Innovations in revision total knee arthroplasty

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Chapter 1

General Introduction

GENERAL INTRODUCTION

Osteoarthritis (OA) is the most common joint disorder in the world. In Western populations it is one of the most frequent causes of pain, loss of function, disability and deterioration of social participation in adults.[1] While OA can occur in almost any joint, knee OA is one of the most prevalent types of osteoarthritis and results in a substantial loss of quality-adjusted life years.[2-4] Risk factors for developing knee OA include increasing age, obesity, female gender, genetic predisposition and previous knee injury.[1,5]

Total knee arthroplasty (TKA) is thought to be the gold standard for the surgical treatment of end-stage OA, with a survival rate of 94% after ten years and good functional results.[6-9] Most patients undergoing TKA are elderly. In 2013 the mean age of patients undergoing TKA in the Netherlands was 68.1 (±9.4) years, and 80% was older than 60 years.[10] The number of younger patients undergoing TKA is growing though, and expectations for the future match this reality.[11,12] The increased numbers of younger patients may have an large impact on healthcare and societal costs due to direct (medical) and indirect (e.g. inability to work) costs. TKA is a highly cost-effective treatment, but less so for the younger population.

The total incidence of TKA is also on the rise, having increased in Western Europe as well as the U.S., Canada, Australia and Korea; further increases are expected.[13-15] The incidence of TKA in the U.S. is expected to grow by 673% between 2005 and 2030.[16] In the Netherlands, the incidence increased 17% in only three years (from 20,539 procedures in 2010 to 24,091 in 2013) and is expected to grow by 52% between 2005 and 2030.[10,11] This rise is attributed to different reasons. Growth of the elderly population and the obesity epidemic are important factors. The disproportional increase in younger patients undergoing TKA may have another explanation: a more active population and the ensuing increase in sports-related injuries may partly explain why increasing numbers of patients under age 65 are receiving a knee prosthesis.[17] A shift in the indications for TKA to include younger

patients may also be explained by the fact that newer prosthetic designs are thought to last longer and withstand higher levels of activity than previous prostheses could.[17]

Despite good results after primary TKA, a significant proportion of patients need to have their knee prosthesis replaced; these revision TKAs (rTKAs) are on the increase and are expected to grow further.[14,16] The number of rTKAs performed in the U.S. is expected to increase by 601% between 2005 and 2030.[16] In the Netherlands, the incidence of rTKA increased by 37% in the last three years (from 1,617 procedures in 2010 to 2,215 in 2013).[10] Reasons for this include the increase in primary TKAs performed and a higher life expectancy of patients.

Main reasons for rTKA as well as re-revision TKA are infection, instability and aseptic loosening of the knee prosthesis.[18,20] Lombardi et al.[19] stated that early mechanisms of failure are primarily due to technical errors. Correct ligamentous balancing and achieving optimal prosthetic alignment during primary and revision TKA are therefore essential for obtaining optimal prosthetic survival. By optimizing the surgical technique, the outcome after TKA may be improved and failure of a knee prosthesis may be prevented.

AIMS OF THIS THESIS

This thesis focuses on new techniques in rTKA and is divided into three parts. The first part focuses on options in knee revision surgery. During rTKA, several choices exist when it comes to type of prosthesis, options for filling up bone defects and whether or not to use intramedullary stems. The second part focuses on alignment measurements in TKA. Achieving optimal knee prosthesis alignment during TKA is essential for good functional outcome and prosthetic survival. Valid and reliable measurements of prosthetic alignment are therefore of major importance. Correct alignment has to be achieved perioperatively when the knee prosthesis is implanted. The last part of the thesis focuses on computer-assisted surgery (CAS) in TKA. This new

technique is developed to help determine the correct prosthesis position during TKA and may therefore improve knee prosthesis alignment.

PART 1: OPTIONS IN KNEE REVISION SURGERY

The goal of both primary and revision TKA is to restore function and stability of the knee joint and to relieve pain. However, rTKA is a more complex surgical procedure than primary TKA and results in worse clinical outcome and shorter survival of the prosthesis.[9,21,26] A major difference between primary and revision TKA lies in the amount of ligamental damage and bone loss, which may lead to instability of the knee joint or fixation problems of the prosthesis.[27,28] Restabilizing the knee joint may therefore be challenging during rTKA. To compensate for ligamental damage, an implant with more constraint is recommended. During primary TKA, a posterior cruciate-retaining (PCR) or posterior stabilized (PS) prosthesis is generally implanted.[29] During rTKA, however, a PS prosthesis, a condylar-constrained knee (CCK) prosthesis or even a rotating-hinge knee (RHK) prosthesis is necessary to obtain a stable knee joint, depending on the severity of ligamental damage.[30,31] Using more constraint also has a downside: the more constraint is used, the more stress arises at the bone-cement interface, which may lead to earlier aseptic loosening of the prosthesis. Hence the minimum degree of constraint necessary is recommended.[32,33] To further reduce the load on the bone-cement interface, intramedullary stems are used in prostheses with more constraint to provide for load sharing.[34,35]

The classification of the Anderson Orthopaedic Research Institute (AORI)[36] is commonly used to classify bone defects in TKA. When it is not possible to achieve a stable basis for a knee prosthesis due to bone defects, augments have to be used. Options for counteracting bone loss include autograft or allograft bone, bone cement, metal augments and trabecular metal cones.[37,40] When larger defects are present, especially when the defect involves the cortical bone, augments alone cannot provide for enough initial

support of the knee prosthesis. In such cases, intramedullary stems are used to provide for load sharing.[40-42] Trabecular Metal (TM) cones are a new option for filling up major bone defects. When a tibial TM cone is implanted, the tibial prosthesis component is generally implanted with a stem extension, to provide for load sharing. A stem extension under the tibial tray may not be mandatory though, as a TM cone might give enough support to the tibial tray and additional load sharing may not be necessary.

Objective of this part of the thesis is to gain insight into different options during rTKA. In **Chapter 2** survival rates are compared between primary and specially designed revision prostheses when implanted during rTKA. **Chapter 3** assesses the mechanical stability of a tibial component implanted with and without a stem when a TM cone is used to fill up major bone defects.

PART 2: ALIGNMENT MEASUREMENTS IN TKA

Achieving optimal prosthetic alignment during TKA is fundamental, since malposition leads to earlier aseptic loosening and revision surgery.[43¬45] Revision TKA has to be prevented, since it is associated with worse functional outcome, pain and shorter survival of the prosthesis.[46-48]

Alignment of the prosthesis can be assessed in three planes: the coronal, sagittal and axial planes. Malalignment of a knee prosthesis in the coronal and sagittal planes is linked to compromised implant survival and functional outcome, increased wear and osteolysis.[44,49-53] Rotational malalignment has a negative effect on patellar tracking, postoperative pain, stability and overall biomechanics of the knee joint.[53-55]

To measure alignment in the coronal and sagittal planes, conventional weight bearing long-leg radiographs are generally used. This 2D measurement technique has some pitfalls. Measured angles may not be correct due to divergence in the horizontal and vertical planes. Moreover, validity of the measurements is easily influenced by the position of the

patient's lower limb during acquisition. Varus or valgus angle, rotation and flexion of the lower limb influence 2D alignment measurements.[56-59] To tackle this issue, 3D measurements using CT-scan or EOS have been developed. Disadvantages of a CT-scan are high levels of radiation, costs and the fact that measurements are non-weight bearing. The EOS system (EOS Imaging, Paris, France)[60] is a new low-dose X-ray device that orthogonally creates 2D long-leg radiographs. It is possible to generate 3D reconstructions based on these 2D images. However, the EOS software for creating 3D reconstructions was initially not developed for assessing alignment of lower limbs containing a knee prosthesis.

Objective of the second part of this thesis is to investigate application of the EOS system to perform knee prosthesis alignment measurements. The reliability and validity of the EOS system when performing such measurements are investigated in **Chapter 4** and **Chapter 5**, respectively. EOS and CAS knee prosthesis alignment measurements are compared in **Chapter 6**.

PART 3: COMPUTER-ASSISTED SURGERY IN TKA

CAS has been developed to improve knee prosthesis alignment. In primary TKA, the use of CAS has shown to improve coronal and sagittal alignment of the knee prosthesis with fewer outliers compared to conventional techniques.[54,61-65] Whether CAS also improves rotational alignment is still a matter of debate.[66] Also, the influence of CAS during rTKA (CAS-rTKA) remains controversial. Only few studies have investigated the influence of CAS-rTKA on postoperative prosthetic alignment, and there are indications that CAS improves coronal and sagittal alignment.[67-71] The effect on rotational alignment has not been investigated yet.

Objective of the last part of this thesis is to gain insight into the influence of CAS during TKA on postoperative alignment. The influence of CAS-TKA on postoperative rotational alignment is assessed in **Chapter**

8. In **Chapter 7** and **Chapter 9** the influence of CAS-rTKA on postoperative alignment in the coronal, sagittal and rotational planes is investigated.

This thesis ends with a general discussion (**Chapter 10**) of the studies presented, including its strengths and limitations, practical implications and recommendations for further research.

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Chapter 2

Poorer survival after a primary implant during revision total knee arthroplasty

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ABSTRACT

Purpose: Revision total knee arthroplasty (rTKA) is a complex procedure. Depending on the degree of ligament and bone damage, either primary or revision implants are used. The purpose of this study was to compare survival rates of primary implants with revision implants when implanted during rTKA.

Methods: A retrospective comparative study was conducted between 1998 and 2009 during which 69 rTKAs were performed on 65 patients. Most common indications for revision were infection (30%), aseptic loosening (25%) and wear/osteolysis (25%). During rTKA, a primary implant was used in nine knees and a revision implant in 60.

Results: Survival of primary implants was 100% at one year, 73% (95% CI: 41-100%) at two years and 44% (95% CI: 7-81%) at five years. Survival of revision implants was 95% (95% CI: 89-100%) at one year, 92% (95% CI: 84-99%) at two years and 92% (95% CI: 84-99%) at five years. Primary implants had a significantly worse survival rate compared to revision implants when implanted during rTKA (P=.039; hazard ratio=4.56 95% CI: 1.08-19.27).

Conclusions: Based on the results, it has to be considered whether primary implants are even an option during rTKA.

INTRODUCTION

Over the past two decades there has been an increase in the number of primary total knee arthroplasties (TKAs) performed.[1,2] Despite good results of primary TKA, the number of revision TKAs (rTKAs) is rising[3] and a further increase in revision procedures in the future is predicted.[4] The demand for revision TKA is expected to double by 2015 and a growth of 601% is predicted for the United States between 2005 and 2030.[4] A similar trend is expected for other Western countries.

Primary implants differ from revision implants in type of insert (constraint) and in the absence of stems and augmentations. During rTKA the surgeon faces greater bone loss and more ligament damage, which may lead to instability of the knee joint.[5,6] To overcome these problems, an implant with more constraint is recommended, and augmentations are commonly used to compensate for bone defects.[7]

Although a posterior cruciate retaining (PCR) or a posterior stabilized (PS) prosthesis is generally implanted during primary TKA,[8] most of the time, an rTKA requires a PS type.[9] Condylar-constrained knee (CCK) and rotating-hinge knee (RHK) types are also commonly used in rTKA.[8-10] When all ligaments are intact and of good quality and bone defects are limited, use of a PCR prosthesis will be sufficient. When only the posterior cruciate is damaged, a PS type is needed. A CCK is chosen when one or both collateral ligaments are inadequate. If medial and/or lateral collaterals and cruciate ligaments are compromised or when a severe deformity exists, a RHK is required.[7,8,11,12] The consequence of using one of these types of revision prosthesis, however, is greater constraint. Higher constraint has negative effects on implant interfaces and is usually counteracted by press-fit stems.[8,13] Hence, the choice of implant type is based on accurate assessment of ligament quality, bone loss and component fixation; the least degree of constraint necessary is recommended.[8,10,14-16]

In handling bone defects, the classification of the Anderson Orthopaedic Research Institute is a useful guide.[17] In type 1 defects, primary prostheses may be used, whereas type 2 or 3 defects necessitate revision

implants. Reasons to opt for a primary implant may also be greater surgeon experience and availability of revision components during the operation when encountering defects and the costs. However, theoretical advantages of using primary implants, such as ease of use, less time and cost savings, may be lost when inadequate reconstruction leads to early loosening.

Previous research has shown that compared with primary TKA, survival following rTKA is poorer.[18-20] The objective of this study was to investigate whether there are differences in survival rates between primary and revision implants when implanted during rTKA.

MATERIALS AND METHODS

Study design and data collection

A retrospective comparative study was conducted. Data on 171 rTKAs performed between January 1998 and December 2009 at our institution were collected retrospectively. The cases were divided into two groups: knees that received a primary implant and knees that received a revision implant. Primary implants were defined as PCR and PS types without the use of stems or augmentations. Revision implants were defined as PS types with the use of stems or augmentations and CCK and RHK types. Survivorship and reason for any reoperation were documented. A telephone call to obtain this information was made to the patients, or to their general practitioner or surviving relative when a patient had died. The study was conducted in accordance with the regulations of the local medical ethical committee.

Study population

Patients with a primary total knee implant who underwent a total revision or reimplantation were included in the study. Excluded were partial revisions, insert replacements, conversions from a unicompartimental prosthesis to a total knee prosthesis and patients who received a tumour prosthesis during revision surgery. Eventually, 69 knees (65 patients) were available for final analysis (Fig. 1). The patient population consisted of 27

men and 38 women, with a mean age of 64.3 (range 30-85) years. Mean time between primary TKA and rTKA was 103.3 (range 2-276) months. The most common reasons for revision were infection (30%), aseptic loosening of one or more components (25%) and wear/osteolysis (25%). During rTKA, nine knees received a primary implant and 60 knees received a revision implant. Of the nine knees receiving a primary implant, three received a NexGen Legacy posterior stabilized (NexGen PS; Zimmer, Warsaw, IN, USA), five an AGC PCR prosthesis (Biomet Inc., Warsaw, IN, USA) and one an LCS rotating platform (PS) prosthesis (Depuy Johnson & Johnson, Warsaw, IN, USA). Sixty revisions were performed with a NexGen revision implant with stems and augmentation. In 37 knees a PS insert was used, in 20 a semiconstrained insert (Legacy Condylar Constrained Knee, LCCK) and in three a rotating-hinge knee (NexGen RHK; Zimmer, Warsaw, IN, USA).

Surgical procedure

Revision TKA was performed by two senior orthopaedic surgeons (SKB and ALB) working at our institution. During rTKA all components were removed and replaced by a primary or revision implant. The medial parapatellar approach was used in all procedures, and all femoral, tibial and patellar components were cemented. Stems were routinely uncemented but a press-fit was used. Infections were treated by two-stage revision. Postoperatively, all patients followed the same protocol with early weight bearing mobilisation permitted in cases with repair of contained defects. Otherwise, this was postponed to six to 12 weeks postoperatively, depending on individual situations.

Statistical analysis

Survival of primary implants used during rTKA was compared with survival of revision implants. The patient who was lost to follow-up was censored using the date of last contact at our hospital. Deceased patients were censored using the date of death. Kaplan-Meier survival analyses were performed to assess the survival of the two types of implant at one, two and five years. To study differences between groups and to adjust for potential confounders

such as age, indication, sex and American Society of Anesthesiologists (ASA) classification, the Cox regression analysis was performed.[21] Additionally, the variables of age, indication (septic or aseptic), sex and ASA classification were assessed for confounding. When the variable was a significant confounder, it was added to the Cox regression. The endpoint for survival following rTKA was defined as repeat revision when one or more of the components was removed or exchanged. Statistical analyses were performed using the PASW software package (version 18, SPSS, Chicago). A p-value of <.05 was considered to be statistically significant.

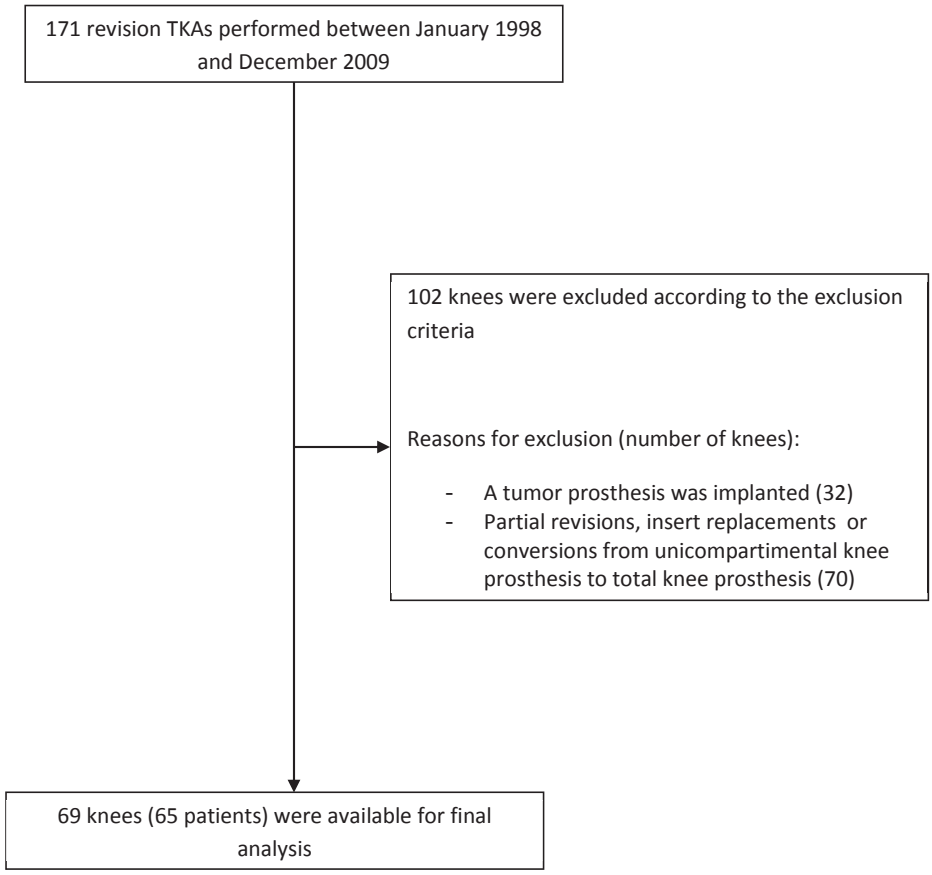

Figure 1. Flow chart of exclusion procedure.

RESULTS

Mean survival of all rTKAs was 58.6 (range 1-161) months. Overall survival of both primary and revision implants was 96% (95% CI: 91-100%) at one year, 89% (95% CI: 82-97%) at two years and 85% (95% CI: 75-94%) at five years. Survival of primary implants was 100% at one year, 73% (95% CI: 41-100%) at two years and 44% (95% CI: 7-81%) at five years. Survival of revision implants was 95% (95% CI: 89-100%) at one year, 92% (95% CI: 84-99%) at two years and 92% (95% CI: 84-99%) at five years. The use of a revision implant during revision surgery had a significantly better survival rate than the primary implant (P=.008; hazard ratio (HR) = 5.87, 95% CI: 1.57-21.90).

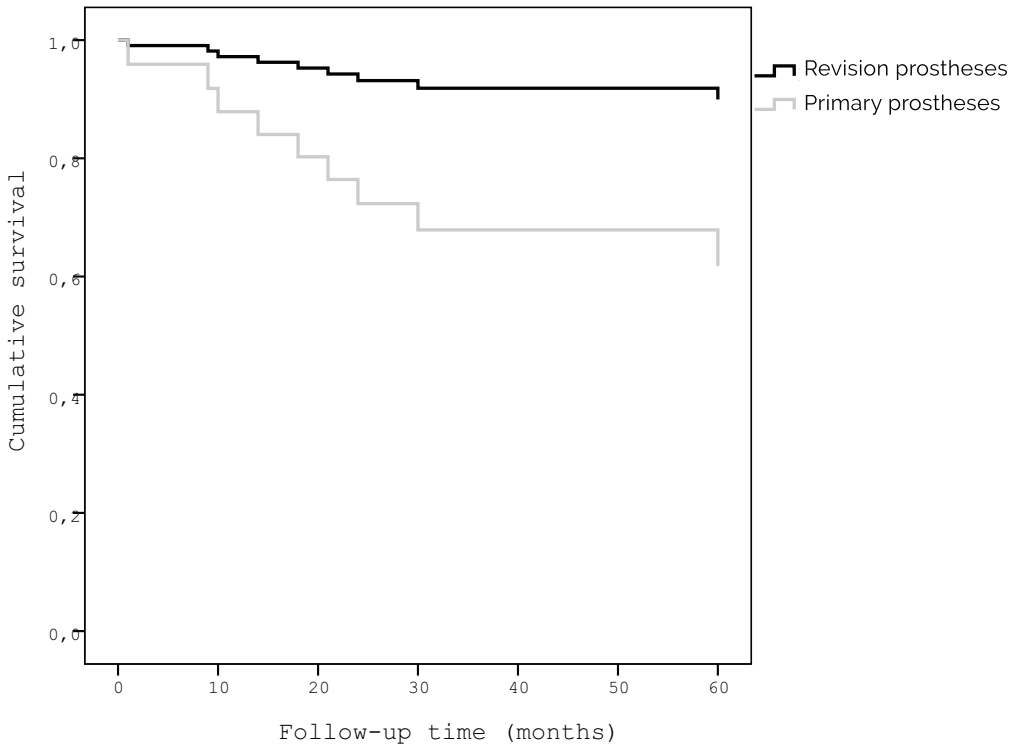

Figure 2. Survival of revision implants. Implants were divided into two groups: primary implants and revision implants. Covariate septic or aseptic indication for revision was added in this Cox regression analysis.

The variables of age, ASA classification and sex were not significant confounders. The variable of indication for rTKA because of sepsis appeared to be a significant confounder. After adding this confounder into the Cox regression analysis, use of a revision implant during rTKA retained a significantly better survival rate than implantation of a primary implant (P=.039; HR=4.56, 95% CI: 1.08-19.27) (Fig. 2).

A total of nine re-operations were assessed in this study. Four primary implants underwent a re-rTKA. Indications were aseptic loosening in two cases and infection in two cases. Five revision implants underwent a re-operation. Three re-rTKAs, one amputation and one arthrodesis were performed. Indications for re-rTKA were aseptic loosening, infection and instability in one case each. Indication for amputation was chronic pain, and infection was the reason for arthrodesis.

DISCUSSION

To our knowledge, this is the first study to investigate survival of primary and revision implants. Over the past two decades, there has been an increase in rTKAs[3] performed, and a further increase is predicted.[4] This has heightened the interest in rTKA and factors that influence the outcome of this procedure. During rTKA, primary and revision implants are used to restore the knee joint. However, little is known about the survival rate of both types of implants following rTKA and whether implanting a primary implant during rTKA is a good option. This study was conducted to compare survival rates of primary implants with revision implants when implanted during rTKA.

Our results show that a primary implant used during rTKA suffers a significantly worse survival rate compared with a revision implant during the revision operation. Overall survival of implants, with repeat rTKA defined as the endpoint, was 96% at one year, 89% at two years and 85% at five years in this study. These results are comparable with rTKA survival in Finland between 1990 and 2002, which showed rates of 95% at two years, 89% at five years and 79% at ten years.[18] Other, generally older, studies report failure rates or poor results of 19- 63% for follow-up periods of five years or less.[22-25]

In this study, five of the 60 revision implants and four of the nine primary implants underwent a re-rTKA. For revision implants, one of the five re-rTKAs was performed for aseptic loosening. For primary implants, two of the four re-rTKAs were performed because of aseptic loosening. Several clinical studies suggest that more constraint leads to earlier aseptic loosening because of more implant-cement-bone stress.[8,13] A characteristic of a revision implant is more constraint; hence, one might expect a higher rate of aseptic loosening. However, in this study, the frequency of aseptic loosening was significantly higher in the group that received a primary implant. Indications for using a primary implant in rTKA are minimal ligament and bone damage. It is possible that these two factors are underestimated in this group of patients. When a primary implant is implanted and more constraint and augmentations are required, this may lead to diminished fixation of prosthesis components to bone, earlier aseptic loosening and thus re-revision. Therefore, it may be questionable whether using a primary implant should be even an option in rTKA, as bone and ligament damage are usually extensive. Which type of revision implant should be advised for what degree of bone and ligament damage is a subject for further study.

Several investigators report that results of septic rTKAs are inferior to aseptic revision.[26-30] In five of the nine revisions where primary implants were used, the reason for revision was infection. In the group of revision implants in our study, 16 of the 60 were done because of an infection; therefore, corrections were made during the survival analysis for septic or aseptic indication.

A strong point of this study is that it adds new knowledge to the scarce literature on survival of primary implants in revision arthroplasty. However, this study also has some limitations. Firstly, a selection bias must be present. Restoration of a knee joint with major ligamental damage and bone loss is a complex procedure. In these cases, a revision implant is always performed. When bone loss and ligamental damage are limited, i.e. cases of Anderson Orthopaedic Research Institute (AORI) type I defects,[31] the surgical procedure is less complex, and one can choose between either a primary or revision implant. Consequently, primary implants are always used in less complex

revision operations, whereas revision implants are also commonly used in more difficult procedures. Secondly, with respect to Cox regression analyses, it is assumed that observations are independent of each other. However, four patients in this study underwent bilateral rTKA, and survival analyses were carried out without taking bilaterality into account. Robertsson et al. reported that the effect of not accounting for bilaterality in knee revision surgery is minute, and that the risk of revision of knee implants can be analysed without consideration for subject dependency.[32] Finally, it can be argued that a limited number of patients was available. Revision surgery is a difficult procedure, and this type of surgery is only performed in specialised centres. Therefore, survival of implants at one, two and five years has a wide confidence interval. Because a growing number of rTKAs is expected, future studies with larger series are necessary to gain more insight into long-term survival and the factors that influence rTKA outcome.

Overall, it can be concluded that despite the relatively small number of patients in this study, primary implants implanted during rTKA have a significantly worse survival rate than revision implants. Choosing the right type of implant in rTKA is a challenging task. Based on results of this study, it has to be considered whether primary implants are even an option during rTKA.

CONFLICT OF INTEREST

Drs. A.L. Boerboom is a paid consultant for Zimmer (Warsaw, IN, USA) for training in knee arthroplasty and computer-assisted surgery. The department receives research institutional support from Stryker (Kalamazoo, Mich., USA) and Zimmer (Warsaw, IN, USA). The other authors declare that they have no conflict of interest.

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Chapter 3

Tibial base plate without stem extension in a Trabecular Metal cone construct

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ABSTRACT

Background: Trabecular metal (TM) cones are designed to fill up major bone defects in total knee arthroplasty. Tibial components can be implanted in combination with a stem, but it is unclear whether this is necessary after reconstruction with a TM cone. Implanting a stem may give extra stability, but may also have negative side-effects.

Questions/purposes: To investigate stability and strain distribution of a tibial plateau reconstruction with a TM cone while the tibial component is implanted with and without a stem, and whether prosthetic stability was influenced by bone mineral density (BMD).

Methods: Tibial revision arthroplasties were performed after reconstruction of an AORI 2B bone defect with TM cones. Plateaus were implanted in seven pairs of cadaveric tibiae; one tibia of each pair was implanted with stem, the other without. All specimens were loaded to one bodyweight alternating between the medial and lateral tibial plateau. Implant-bone micro motions, bone strains, BMD and correlations were measured and/or calculated.

Results: Tibial components without a stem showed only more varus tilt (difference in median 0.14˚ ($P<0.05$), but this was not considered clinically relevant. Strain distribution did not differ. BMD only had an effect on the anterior/posterior tilt (:-0.72 ($P<0.01$).

Conclusions: Tibial components, with or without a stem, which are implanted after reconstruction of major bone defects using TM cones produce very similar biomechanical conditions in terms of stability and strain distribution.

Clinical relevance: Additional stem extension of the tibial component may not be required after reconstruction of major bone defects using TM cones.

INTRODUCTION

Major bone defects are frequently seen in revision total knee arthroplasty (rTKA). Reasons for this may be design and removal of the primary prosthesis, original disease process, mechanism of failure and technical problems during the procedure. Reconstruction of the knee joint and acquiring correct prosthetic alignment during rTKA therefore constitute a challenging task.

Types 2B and 3 bone defects according to the classification of the Anderson Orthopedic Research Institute (AORI)[1-4] are commonly seen during rTKA and reconstruction of these major bone defects is usually done with metal augmentations in combination with a stem,[5-7] which is shown to provide a mechanically stable reconstruction.[8-10] However, literature shows that a stem may cause increased stress at the distal part of the stem and a decrease of stress at the proximal part.[11] If enhanced stress-shielding occurs, adverse bone remodeling may follow in the long term, possibly influencing component fixation and inducing fractures.[12-14] Another disadvantage of the use of stems is elevated stress at the tip of the stem, which is associated with pain, lower postoperative clinical outcome and increased risk of periprosthetic fracture.[15]

Trabecular metal (TM) cones[16,17] are a relatively new option for reconstruction of major bone defects during TKA. TM is reported to be biocompatible, corrosion-resistant and highly porous, with an average pore diameter of approximately 400 µm.[18,19] Because of the porous structure ingrowth is encouraged and cement fixation is solid.[20] TM cones are available in various designs and sizes, in order to adjust to the type and size of the defect and bone. Several studies have shown good short-term functional results with evidence of osseo-integration when a TM cone was used.[21-27] Tibial TM cones are designed to be impacted into the proximal tibia, to allow for osseous ingrowth and provide proximal support. After reconstruction of the proximal tibia, the tibial component is cemented in this cone and usually implanted with a stem. However, whether a stem is mandatory when a TM cone is used hasn't been investigated yet. A tibial TM cone is designed to enhance the carrying capacity of the metaphyseal bone of the proximal tibia,

thereby rendering a situation as in a primary arthroplasty. Hence a stem under the tibial base plate might not be needed to provide mechanical stability in combination with a tibial TM cone. Moreover, without use of a stem proximal stress-shielding may be reduced and it would save the costs of the stem.

The purposes of this study are thus to investigate stability and strain distribution of tibial reconstructions with a base plate with and without a stem cemented on a TM cone. Additionally, it was investigated whether prosthetic stability was likely to be influenced by bone mineral density (BMD).

MATERIALS AND METHODS

A cadaveric study was conducted in which seven pairs of fresh frozen tibial bones (four male and three female, mean age 82 years (range 70–89)) were disarticulated at the ankle and stripped of all soft tissues. The distal ends of the tibiae were potted in bone cement. Bone mineral density (BMD) of the tibiae was determined using a calibrated CT-scan and in-house software (DCMTK). Two spherical volumes of interest with a diameter of 11.4 mm in the medial and lateral proximal tibia were selected for the measurements. The averaged BMD of these two regions was later used to assess whether there was any effect of BMD on the biomechanical output parameters.

In each tibia, bone cuts were made as if a primary knee prosthesis were to be placed. Next, an AORI type-2b bone defect of approximately 10 mm^3 was created at each medial and lateral side, as demonstrated in Figure 1. In this way, the situation after removal of the primary prosthesis was simulated. The bone defect was first created in one cadaveric bone and served as a reference to create similar bone defects in the other cadaveric bones. For each pair of tibiae, one tibia was reconstructed using a porous tantalum metaphyseal full tibial cone (Trabecular Metal (TM), Zimmer Inc., Warsaw, IN, USA). After this reconstruction a NexGen® tibial base plate was implanted with a 100-mm press-fit stem extension (Zimmer Inc., Warsaw, IN, USA) and provided with a polyethylene insert (Legacy posterior stabilized (LPS) flex, 10-12 mm; Zimmer Inc., Warsaw, IN, USA). The other tibia was reconstructed using the same TM cone and NexGen® tibial component and polyethylene

insert, but no stem extension was used. All tibial components were cemented using bone cement (Refobacin® revision bone cement with clindamycin and gentamicin, Biomet Inc., Warsaw, IN, USA). Only the proximal part of the tibial component up to the connection of the stem was cemented. As bone ingrowth could not be expected and TM cones are frequently implanted using bone cement in clinical practice, the TM cones were also fixed by using bone cement in our experimental setup (Fig. 1). Preparation of the tibiae and implantation of the components was performed by one orthopedic surgeon (ALB). Allocation of whether the left or the right tibia was implanted with a stem was randomized by using a computer-generated list.

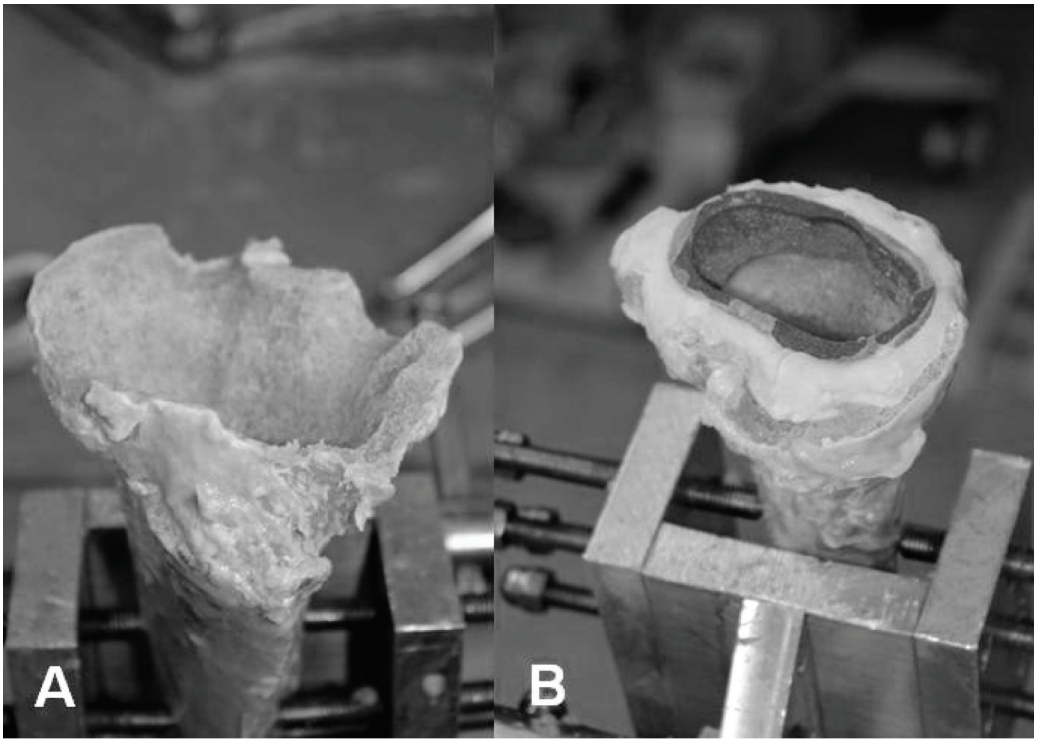


Figure 1. (A) An example of the created bone defect. (B) Reconstruction of a bone defect using a trabecular metal cone.

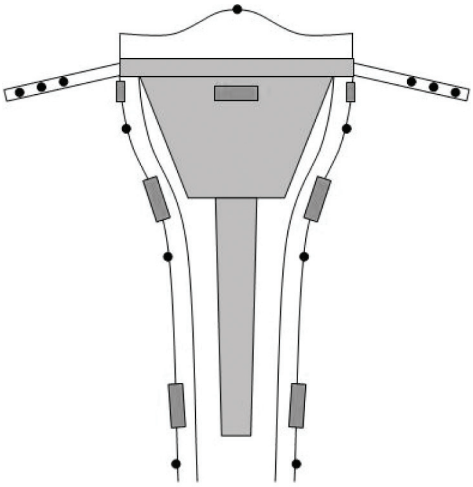
The next step was to test the cadaveric reconstructions for stability. RSA was used to determine migration and rotation of the components. Seven tantalum pellets (0.8 mm diameter) were glued to the tibial component and six tantalum pellets were placed into the shaft of the proximal and distal tibia

in standard positions (Fig. 2). The tip of the polyethylene insert was chosen as the origin of the coordinate system relative to which rotations and translations of the component were expressed. Stereoradiograms of the medially and laterally loaded situations were made before loading and after 10,000 loading cycles. The radiograms were digitized manually and analyzed using RSA software (RSA-CMS, Medis, Leiden, The Netherlands). In a previously conducted knee study the estimated error for the same RSA analysis was less than 50 µm for repeated measurements, with a standard deviation of 0.1 mm.[28] Endpoints of the RSA were translation and rotation along the X-, Y- and Z-axes. Translations along these axes were defined as medial/lateral translation, superior/inferior translation and anterior/posterior translation, respectively. Rotations along the X-, Y- and Z-axes were defined as anterior/posterior tilt, internal/external rotation and varus/valgus tilt, respectively. Total translation (TT) was also calculated using the following equation: $TT = \sqrt{(x^2+y^2+z^2)}$.[29] The TT can be considered as a close equivalent to maximum total point motion (MTPM).[29,30] We calculated the TT because the MTPM was not calculated with the RSA software used in this study.

To evaluate strain distributions between the tibiae with and without stem, seven strain gauges (type YFLA-5, Tokyo Sokki Kenkyujo Co., Ltd., Tokyo) were used. The gauges were positioned horizontally on the cortex 15 mm under the tibial plateau at the medial, anterior and lateral side, and vertically at the connection of the TM cone to the stem and 5 mm proximally of the tip of the stem on the medial and lateral sides (Fig. 2). The contralateral tibia served as reference for the tibiae in which no stem was used. All strain gauges were connected to an amplifier and a computer to record data using monitoring software (quickDAQ 1.5.0.6, Data Translation, Inc, Marlboro, MA, USA). Strain was recorded during the entire loading session of 10,000 cycles.

The tibiae were clamped into a testing machine (MTS, model 458020, MTS Systems Corporation, Minneapolis, MN, USA) with the tibial plateau parallel to the working bench (Fig. 3). A unicondylar axial load alternating between the medial and lateral parts of the tibial plateau was performed. The load cycled between zero and 700 N at a frequency of 1 Hz in a series of eight loading cycles, i.e. the medial and lateral parts of the tibial plateau

were both loaded eight times, thus applying varus-valgus stress to test for maximal instability of the reconstruction. A previous study at the same institution was conducted with the same setup.[31]



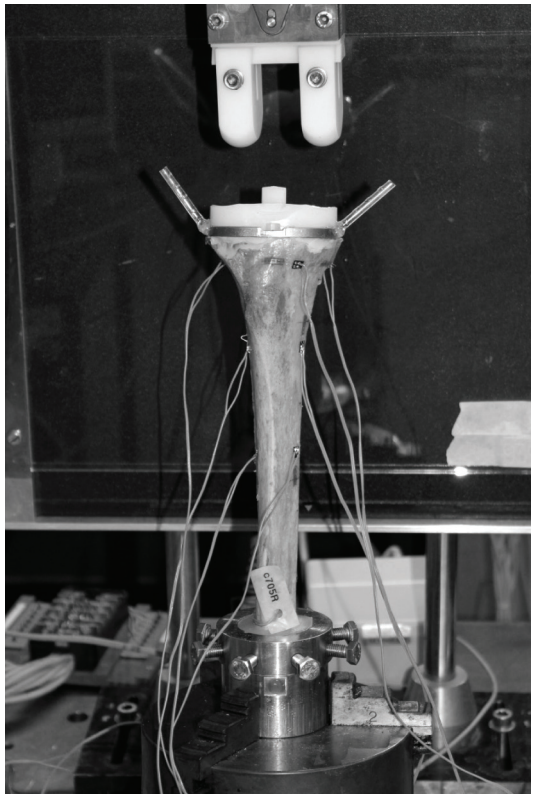


Figure 2. (left) Schematic representation of the locations of the tantalum pellets and strain gauges. The black dots represent the tantalum pellets and the rectangles represent the strain gauges.

Figure 3. (right) The experimental setup.

Statistical analyses

All statistical analyses were performed using the PASW software package (version 19, SPSS, Chicago). Potential differences between the two groups in rotation, translation and TT for both the medially and laterally loaded situations after 10,000 cycles were investigated using the paired Wilcoxon signed rank test. The absolute differences between the medially and

laterally loaded RSA measurements and the TT for these differences were also compared between the two groups using the paired Wilcoxon signed rank test. We hypothesized that the difference in rotation or translation between the medially and laterally loaded stereoradiograms may serve as a measure of instability of the construction. The paired Wilcoxon signed rank test was also used to compare the minimal and maximal strains at the different levels between the tibiae with and without stem. The difference between the minimal and maximal strains per level in the last 32 cycles (equal to four alternating configurations of medial and lateral load) of the loading session was also compared. Spearman's correlation coefficient was used to determine the correlation between bone mineral density and the differences in rotation, translation and TT between the medially and laterally loaded situations. The correlation coefficients were interpreted according to the benchmarks described by Domholdt[32]: 0.90-1.00 represents a very strong correlation, 0.70-0.89 a strong correlation, 0.50-0.69 moderate, 0.26-0.49 weak and 0.00-0.25 represents little if any correlation.[32] A p-value <.05 was considered to indicate statistical significance.

RESULTS

Implanting the prosthetic material caused a fissure in one of the proximal tibiae. During loading, the proximal part of this tibia broke off. This tibia and the matching contralateral tibia were therefore excluded from further analysis. None of the other tibial components migrated visually during the loading sessions, hence data of six pairs of tibiae were used for further analysis.

No significant differences were found for anterior/posterior tilt or internal/external rotation between both groups after 10,000 cycles (Table 1). For varus/valgus tilt a minimal yet significant difference was found for the laterally loaded RSA measurements. The group without a stem showed more varus tilt than the group with a stem after 10,000 cycles (P=0.046). No significant difference was found for the medially loaded RSA measurements (Table 1). Translation in the three directions and TT showed no significant differences between the two groups (Table 1). When comparing the medially

		anterior/posterior tilt				internal/external rotation				varus/valgus tilt							
stem/no stem	loading	median	min	max	p-value	median	min	max	p-value	median	min	max	p-value				
stem	medially	0.075	0.043	0.533		-0.007	-0.421	0.037		-0.074	-0.185	0.111					
no stem	medially	-0.063	-1.383	0.326	0.12	0.047	-0.158	0.177	0.17	0.064	-0.360	0.742	0.25				
stem	laterally	0.057	-0.113	0.244		0.024	-0.256	0.093		-0.047	-0.160	0.043					
no stem	laterally	-0.004	-1.389	0.335	0.25	0.093	-0.166	0.392	0.46	0.093	-0.094	0.793	<0.05*				
		medial/lateral translation				superior/inferior translation				anterior/posterior translation				TT			
stem/no stem	loading	median	min	max	p-value	median	min	max	p-value	median	min	max	p-value	median	min	max	p-value
stem	medially	0.066	-0.062	0.225		0.188	-0.182	0.487		0.136	0.430	-0.129		0.352	0.134	0.621	
no stem	medially	-0.008	-0.240	0.381	0.25	-0.001	-0.323	0.974	0.75	0.052	0.259	-0.168	0.60	0.364	0.063	0.978	0.92
stem	laterally	0.009	-0.169	0.160		0.055	-0.317	0.206		0.027	0.305	-0.192		0.339	0.005	0.434	
no stem	laterally	-0.186	-0.289	0.230	0.46	0.039	-0.263	0.133	0.92	0.010	0.336	-0.272	0.35	0.291	0.194	0.714	0.60

Table 1. Median, minimal and maximal rotations and translations in the three axes and total translation (TT) after 10,000 cycles. Rotation is stated in degrees (°) and translation in millimeters (mm). An * indicates significant differences.

and laterally loaded stereoradiograms after 10,000 cycles, no significant differences in rotation or translation in any of the three directions were found (Table 2). TT did not show any significant differences between the two groups when comparing the medially and laterally loaded RSA measurements (Table 2).

A similar strain pattern was found for all strain gauges. An example of the strain pattern during loading is shown in Figure 4. Neither minimal strains (dip of line chart) nor maximal strains (peak of line chart) showed any significant difference between both groups for any of the locations (proximally, connection of cone to the stem, or distally) (Table 3). No significant differences were found regarding the difference between the minimal and maximal strains (differences between peak and dip of line chart) between the two groups (Table 4).

Figure 4. An example of the strain pattern during biomechanical testing. The load cycled between zero and 700 N at a frequency of 1 Hz in series of eight loading cycles.

Mean BMD of the cadavers was 114.7 (SD: 64; range: 30–213). The tibia that fractured during loading had a BMD of 112.7 mg/mm^3. As mentioned earlier, this tibia and the matching contralateral tibia were excluded from further analysis. The correlation between the BMD and the difference between the medially and laterally loaded RSA measurements for anterior/posterior tilt was strong (: 0.72, P<0.01) (Fig. 5), indicating that for this direction more motion was produced for lower-density bones. After exclusion of one outlier (marked

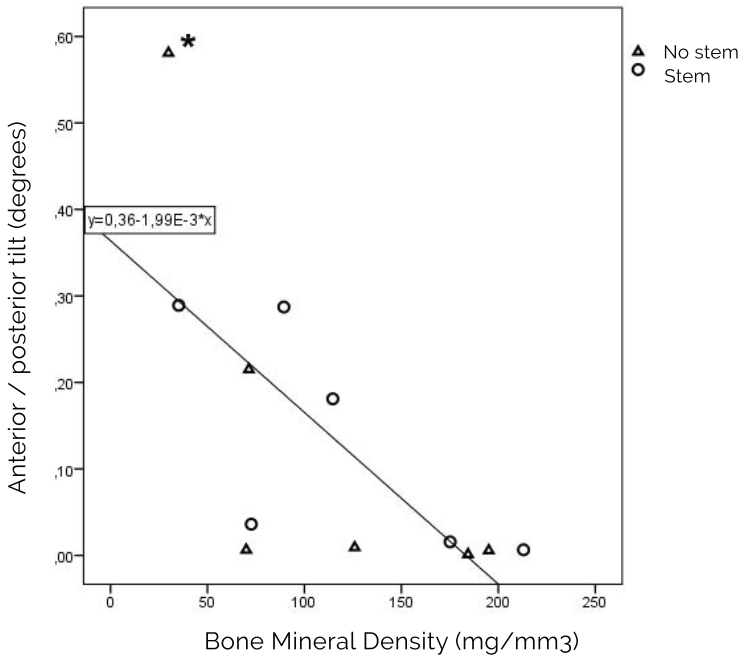


Fig. 5 Scatter dot showing the correlation and correlation line between the bone mineral density and the difference between the medially and laterally loaded RSA measurements for anterior/posterior tilt. The * marks the outlier.

Table 2. Median, minimal and maximal differences between the medially and laterally loaded RSA measurements after 10,000 cycles for rotations and translations in the three axes and total translation (TT). Rotation is stated in degrees (°) and translation in millimeters (mm).

	Stem/no stem	Median	Minimum	Maximum	P-value
Anterior/posterior tilt	Stem	0.109	0.006	0.289	
Anterior/posterior tilt	No stem	0.008	0.001	0.581	0.35
Internal/external rotation	Stem	0.063	0.010	0.177	
Internal/external rotation	No stem	0.197	0.093	0.337	0.17
Varus/valgus tilt	Stem	0.103	0.001	0.228	
Varus/valgus tilt	No stem	0.130	0.051	0.377	0.35
Medial/lateral translation	Stem	0.120	0.041	0.333	
Medial/lateral translation	No stem	0.171	0.050	0.611	0.35
Superior/inferior translation	Stem	0.254	0.007	0.580	
Superior/inferior translation	No stem	0.201	0.018	1.237	0.75
Anterior/posterior translation	Stem	0.092	0.012	0.446	
Anterior/posterior translation	No stem	0.091	0.000	0.146	0.35
TT	Stem	0.291	0.194	0.714	
TT	No stem	0.377	0.130	1.252	0.46

Table 3. Median, minimum and maximum of the minimal and maximal strains measured during the last 32 cycles of the loading session. Strain is stated in microstrains (μstrain).

Strains proximally (medial, anterior and lateral)						
Stem/no stem	Cycles	Strain	Median	Minimum	Maximum	P-value
Stem	10,000	Medial min	39.57	-97.62	145.11	
No stem	10,000	Medial min	27.70	-153.02	332.42	0.92
Stem	10,000	Medial max	76.51	-21.11	179.40	
No stem	10,000	Medial max	39.57	-306.04	129.28	0.12
Stem	10,000	Anterior min	19.79	-142.47	203.15	
No stem	10,000	Anterior min	25.06	-108.17	253.28	0.60
Stem	10,000	Anterior max	-42.21	-108.17	60.68	
No stem	10,000	Anterior max	26.38	-163.57	150.38	0.60
Stem	10,000	Lateral min	146.42	-5.28	1155.57	
No stem	10,000	Lateral min	26.38	-1216.25	1290.12	0.25
Stem	10,000	Lateral max	178.08	65.96	736.08	
No stem	10,000	Lateral max	40.89	-817.87	284.93	0.12
Strains at the level of the connection of cone to stem (medial and lateral)						
Stem/no stem	Cycles	Strain	Median	Minimum	Maximum	P-value
Stem	10,000	Medial min	48.81	-282.30	356.17	
No stem	10,000	Medial min	110.81	-36.94	530.29	0.46
Stem	10,000	Medial max	87.06	60.68	332.42	
No stem	10,000	Medial max	75.19	-18.47	1408.84	0.92
Stem	10,000	Lateral min	-7.92	-124.00	517.10	
No stem	10,000	Lateral min	7.92	-226.89	110.81	0.46
Stem	10,000	Lateral max	34.30	-81.79	229.53	
No stem	10,000	Lateral max	17.15	-197.87	514.46	0.60
Strains distally (medial and lateral)						
Stem/no stem	Cycles	Strain	Median	Minimum	Maximum	P-value
Stem	10,000	Medial min	0.00	-44.85	274.38	
No stem	10,000	Medial min	-1.32	-522.38	44.85	0.12
Stem	10,000	Medial max	97.62	34.30	498.63	
No stem	10,000	Medial max	75.19	-2.64	321.87	0.17
Stem	10,000	Lateral min	-48.81	-279.66	31.66	
No stem	10,000	Lateral min	-30.34	-139.83	0.00	0.89
Stem	10,000	Lateral max	27.70	-29.02	63.32	
No stem	10,000	Lateral max	19.79	-34.30	474.89	0.60

with an * in Fig. 5), correlation was moderate and significant (: 0.64, P<0.04). Little if any correlation existed for internal/external rotation and varus/valgus tilt (:<0.10, P>0.80). There was little if any correlation between the BMD and the difference between the medially and laterally loaded RSA measurements for medial/lateral translation (:0.21, P=0.51), a moderate and non-significant correlation for superior/inferior translation (:0.50, P=0.10), and a weak and non-significant correlation for anterior/posterior translation (:0.25, P=0.43). The correlation between the BMD and the TT of the difference between the medially and laterally loaded measurements was moderate and non-significant (:0.50, P=0.10).

Table 4. Median, minimal and maximal difference in strain between the minimal and maximal strains measured during the last 32 cycles of the loading session. Strain is stated in microstrains (μstrain).

Location of strain gauge	Stem /no stem	Median	Minimum	Maximum	P-value
Proximal medial	Stem	-13.19	-176.77	42.21	
Proximal medial	No stem	64.64	-23.75	203.15	0.35
Proximal anterior	Stem	22.43	-68.60	142.47	
Proximal anterior	No stem	50.13	-47.490	102.89	0.75
Proximal lateral	Stem	5.28	-271.74	419.49	
Proximal lateral	No stem	-14.51	-398.380	1005.18	0.92
Cone-stem medial	Stem	-30.34	-377.27	52.77	
Cone-stem medial	No stem	-9.23	-878.55	68.60	0.75
Cone-stem lateral	Stem	-21.11	-182.04	287.57	
Cone-stem lateral	No stem	-27.70	-461.70	2.64	0.46
Distal medial	Stem	-39.57	-532.93	168.85	
Distal medial	No stem	-52.77	-844.25	13.19	0.46
Distal lateral	Stem	-58.04	-342.98	0.00	
Distal lateral	No stem	-50.13	-614.72	2.64	0.92

DISCUSSION

TM cones are designed to fill up bone defects during TKA. However, it is unclear whether tibial components should be implanted with or without a stem after reconstruction of bone defects (AORI 2B/3) using a TM cone. Aim was therefore to investigate stability and strain distribution of a tibial plateau reconstruction with a TM cone while the tibial component was implanted with and without a stem. We also questioned whether prosthetic stability was influenced by BMD.

Results of this study showed no evidence that a stem creates benefit and improves stability when a tibial component is implanted in a TM cone. Results of RSA measurements showed no difference between both groups, indicating that both constructions are stable. To our knowledge, this is the first study to investigate stability of a tibial reconstruction with a TM cone and a tibial base plate without stem extension. Results of RSA analysis only showed a significant difference for varus/valgus tilt of the laterally loaded RSA measurements. The cone without a stem showed more varus tilt than the cone implanted with a stem. Differences were small though. The difference between the medians of both groups was only 0.14˚, and the range was

0.20˚ and 0.89˚ for tibial components with and without a stem, respectively. Since these differences were extremely small, they obviously lacked clinical significance. Rotations and translations in the other directions did not show significant differences between the two groups. We calculated differences between the medially and laterally loaded RSA measurements, as this may also give an indication of instability, but this showed no differences either.

Advantages of using stems are resistance of the tibial component to shear loads, reduced tibial lift-off, and increased stability leading to reducing micro-motion. Potential disadvantages include stress-shielding with associated reduction in BMD, risk of subsidence and loosening, periprosthetic fracture and end-of-stem pain.[33] *In vitro* studies have demonstrated a decrease in proximal tibial strain and increase in strain at the distal tip of the stem when a stem was used.[11,14] In a study by Bourne et al.[14] it was concluded that tibial components should have either no short intramedullary stem or only a short one, due to negative side-effects. In our study we did not find differences in strain distribution between the two groups. Reason for this may be that we analyzed bones with severe defects and reconstructed those with the cones. Apparently the addition of the stem did not add to stability or to load transfer, therefore no strain increase at the tip of the stem or decrease at the proximal tibia was observed. This finding is consistent with our results of the RSA analysis, showing that a base plate without stem in a TM cone is a stable mechanical construction.

In this study, a low BMD strongly correlated with a larger difference between the medially and laterally loaded RSA measurements for anterior/posterior tilt. We hypothesized that a greater difference between these measurements could be an indication of instability. A low BMD may thus theoretically decrease stability of the construction. Even though the correlation between the BMD and anterior/posterior tilt was strong and significant, maximum difference in anterior/posterior tilt was only 0.58˚. Such differences are very small and not considered clinically important. For other rotations and translations, correlations with BMD ranged from moderate to weak and were non-significant. It is therefore assumed that the results of this study are representative. Patients who undergo rTKA in general practice tend

to be older, so variety in BMD can also be expected. Moreover, analyses were done in pairs (left and right tibia) per cadaver, thereby facilitating investigation of the effect of the stem despite the variability in BMD.

This study has some limitations. First of all, design was a biomechanical *in vitro* study using cadaveric bone. Forces and number of cycles applied are a simplification of the situation *in vivo*. This notwithstanding, aim of this study was to investigate stability of the proximal tibia after bone defect repair with a tibial TM cone, for which this setup is a suitable design. Several *in vivo* studies have reported good short-term functional and radiological outcome after reconstruction of bone defects using TM cones in TKA with use of stem extensions.[25,27,34-36] And yet, *in vivo* studies have to be conducted to gain insight into radiological and functional effects when a tibial component is implanted without a stem after reconstruction with a TM cone. Secondly, tibial TM cones in this study were implanted using bone cement. The porous structure of TM encourages bone ingrowth and can be implanted without the use of cement. From clinical experience we have found that around 50% of the implanted tibial TM cones in our hospital use bone cement. An uncemented cone has to fit exactly when implanted, otherwise cement has to be used. Since bone ingrowth could obviously not happen in this study and TM cones are also placed using bone cement in clinical practice, we decided to implant all TM cones using bone cement. In this way, homogeneity of the procedure is achieved and one could imagine interpreting the findings for the cementless TM cone applications as if ingrowth had occurred — as would be the case in clinical practice. Thirdly, the cadaveric bones used varied in BMD, and age of the cadavers was relatively old. This is inherent to the use of cadaveric bone, but also similar to the patient population of rTKA. BMD appeared to influence only anterior/posterior tilt. Stability in other directions was not influenced.

In conclusion, this study suggests that additional stem extension of the tibial component may not be required. *In vivo* studies have to be performed to gain insight into the radiological and functional effects when a tibial component is implanted without a stem after reconstruction with a TM cone.

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CONFLICT OF INTEREST

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Chapter 4

Assessment of prosthesis alignment after revision total knee arthroplasty using EOS 2D and 3D imaging: A reliability study

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ABSTRACT

Introduction: A new low-dose X-ray device, called EOS, has been introduced for determining lower-limb alignment in 2D and 3D. Reliability has not yet been assessed when using EOS on lower limbs containing a knee prosthesis. Therefore purpose of this study was to determine intraobserver and interobserver reliability of EOS 2D and 3D knee prosthesis alignment measurements after revision total knee arthroplasty (rTKA).

Methods: Forty anteroposterior and lateral images of 37 rTKA patients were included. Two observers independently performed measurements on these images twice. Varus/valgus angles were measured in 2D (VV2D) and 3D (VV3D). Intraclass correlation coefficients and the Bland & Altman method were used to determine reliability. T-tests were used to test potential differences.

Results: Intraobserver and interobserver reliability were excellent for VV2D and VV3D. No significant difference or bias between the first and second measurements or the two observers was found. A significant mean and absolute difference of respectively 1.00° and 1.61° existed between 2D and 3D measurements.

Conclusions: EOS provides reliable varus/valgus measurements in 2D and 3D for the alignment of the knee joint with a knee prosthesis. However, significant differences exist between varus/valgus measurements in 2D and 3D.

INTRODUCTION

Achieving optimal prosthetic alignment during total knee arthroplasty (TKA) is an essential part of the surgical procedure. Malpositioning of a knee prosthesis in the coronal plane causes earlier loosening and revision surgery.[1] Revision TKA (rTKA) has to be prevented, as this is associated with worse functional outcome and prosthesis survival.[2,3] Proper alignment in the coronal plane is associated with less pain, better knee function, faster rehabilitation and improved quality of life.[4,5] Optimal coronal alignment is considered ≤3˚ varus or valgus.[6]

Conventional weight bearing radiographs are generally used to measure alignment in the coronal and sagittal planes. Proportions and angles may not be correct though, given the divergence in the vertical and horizontal planes. A computed tomography (CT) scanogram can also be used to evaluate prosthetic alignment in the coronal, sagittal and rotational planes. However, due to high levels of radiation and high costs it cannot be used routinely. Moreover, with a CT-scan it is not possible to obtain images of the leg in weight bearing position.

The EOS system has been developed for the evaluation of prosthetic alignment (EOS Imaging, Paris, France).[7] With this biplanar low-dose X-ray technique, orthogonally made long-leg 2D radiographs and 3D reconstructions can be obtained. Major advantages are that images of the leg are obtained on a 1:1 scale with an amount of radiation 800-1000 times lower than CT-scans and 10 times lower than conventional X-rays.[7,8] However, the EOS software for creating 3D reconstructions is developed for lower limbs without knee prosthetic material. When a knee prosthesis is *in situ*, several anatomical reference points have disappeared or changed, making it difficult to mark reference points as described by the measurement protocol. Therefore, the measurement protocol was adjusted. Reliability of this protocol have not been investigated yet.

Purpose of this study was to determine intraobserver and interobserver reliability of 2D and 3D knee prosthesis alignment measurements after rTKA using EOS. As a secondary outcome we assessed whether significant differences existed between 2D and 3D measurements.

MATERIALS AND METHODS

Fifty-four patients who underwent rTKA between January 1998 and November 2009 and who were available for the acquisition of EOS images between November 2009 and May 2010 were included. An anteroposterior (AP) and lateral (LAT) image of the operated leg was made with the EOS stereography system at the Radiology Department of our hospital as part of the standard follow-up protocol for rTKA. In accordance to regulations of the Medical Ethical Review Board of University Medical Center Groningen, patients were informed about the fact that data of their radiographs could be used for scientific research. If patients had objections to the use of their data these data were not included in the study.

Patients were positioned on the EOS platform in standing position with the right foot 10 cm in front of the left foot. SterEOS software (EOS Imaging, Paris, France) was used to take 2D measurements of the AP images and 3D measurements of the AP and LAT images. The images were anonymized by removing names, patient numbers and birth dates. The guidelines for taking measurements as provided by the manufacturer were followed.[9] Since several landmarks disappear or change when a knee prosthesis is *in situ*, the observers made the following agreements on marking the landmarks:

- Instead of the center of tibial spines, the center of the tibial plateau is chosen;
- Instead of marking the distal femoral notch, the center of the femoral component is marked;
- Instead of marking the anatomic femoral condyles, the condyles of the femoral component are marked.

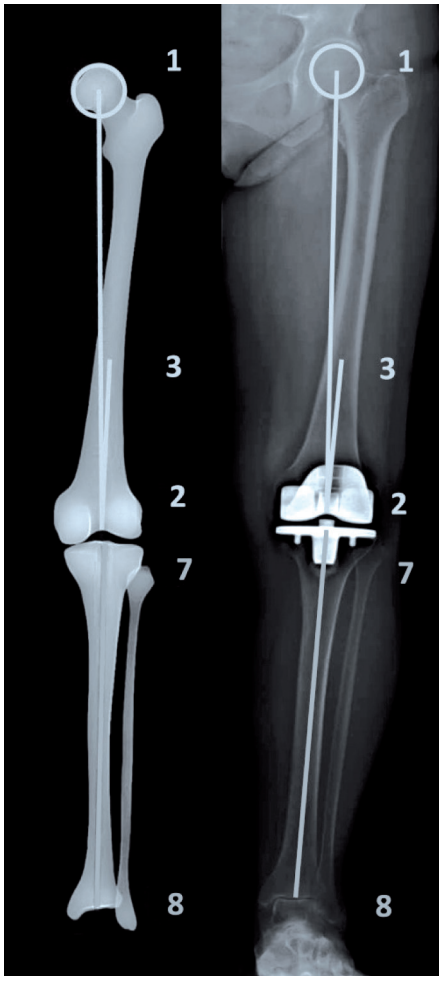
In order to calculate coronal and sagittal alignment parameters of the lower limb in 2D and 3D, the "lower limb alignment" mode is used. The first step is to define the left or right lower limb and to choose the modeling "lower limb alignment" mode. Next, identification of the lower limb on the AP and LAT images is done in 10 steps (Fig. 1 and 2):

Femur:

- Center of femoral head (points 1 and 4);
- Center of the distal femoral notch (points 2 and 5);
- Center of the diaphysis in its distal third (points 3 and 6).

Tibia:

- Center of the tibial spines. When a knee prosthesis is in situ the tibial spines disappear, therefore the center of the tibial plateau is chosen and the axis from the center of the ankle to the center of the tibial plateau represents the anatomical axis of the tibia (points 7 and 9);
- Center of the distal articular surface in the upper ankle joint (points 8 and 10).



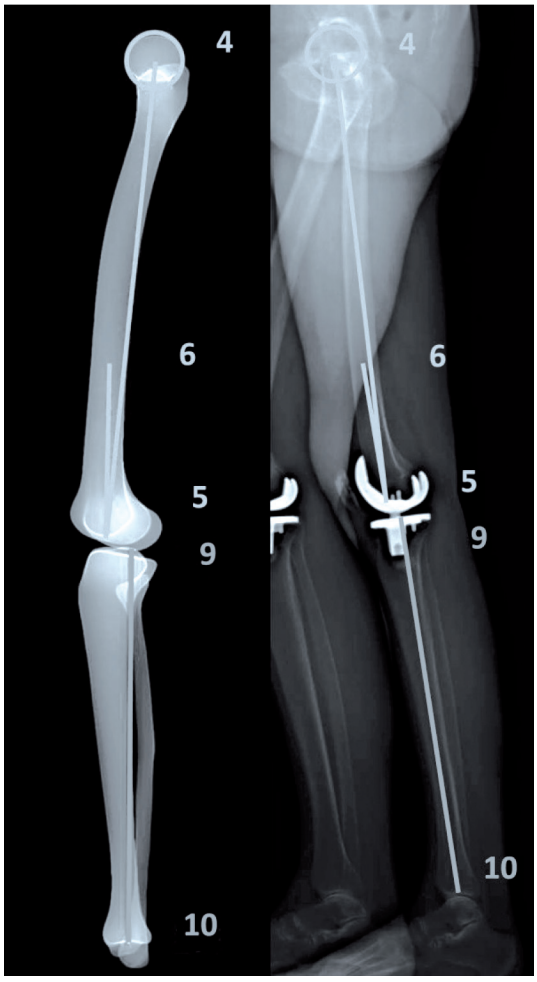


Figure 1 (left). Identification of the lower limb on the frontal image
Figure 2 (right). Identification of the lower limb on the lateral image

The next step is adjustment of the landmarks in four steps (Fig. 3):

1. Adjustment of the position of the sphere of the femoral head in both views. It is possible to enlarge or minimize the size of the sphere according to the size and shape of the femoral head, in order to mark the center of the femoral head as precisely as possible;
2. Adjustment of the point in the center of the distal third of the diaphysis of the femur;
3. Adjustment of the position of the point in the center of the femoral notch and tibial plateau, and marking of the femoral condyles. The condyles have to be identified on the AP and LAT images using the two spheres. It is possible to adjust the size of the spheres, according to the size of the condyles. On the AP image the center of the spheres has to be located in the center of each condyle. On the LAT image the spheres have to be tangent to the posterior part of the condyles. It is important not to confuse the medial with the lateral condyles. In order to identify the right condyle, the epipolar line is used to differentiate between the two condyles by observing the correspondence of condylar height on both the AP and the LAT image;
4. Adjustment of the reference point in the center of the distal articular surface on the AP and LAT images.

VV2D is the angle between the mechanical axis of the femur (axis between points 1 and 2) and the tibia (axis between points 7 and 8) on the AP image (Fig. 1). For the 3D measurement, the points marked on the AP (Fig. 1) and LAT (Fig. 2) images as described above are combined to generate the mechanical axes of femur and tibia. VV3D is the angle between the three-dimensional mechanical axis of the femur (axis between points 1–4 and 2–5) and tibia (axis between point 7–9 and 8–10).

Primary outcome measurement is the varus/valgus angle (VV) (angle between the mechanical axes of femur and tibia) in 2D (VV2D) and 3D (VV3D) because of its clinical importance. A positive value indicates valgus and a negative value indicates varus.

An independent researcher randomly numbered all images twice. In this way, two blinded sets of 40 AP and LAT images each were composed. Two observers (observer A and observer B) separately analyzed both sets of 40 images twice. Both observers were experienced in taking the measurements in 2D and 3D prior to the study.

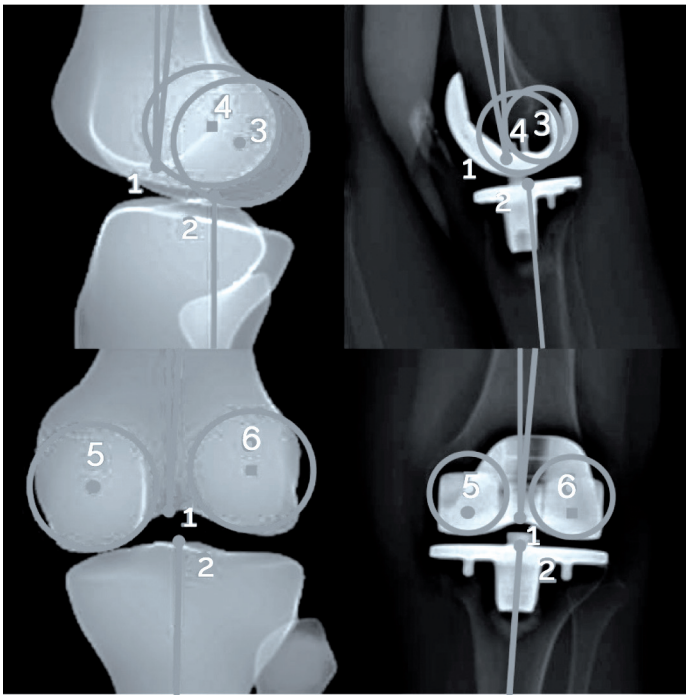


Figure 3. Adjustment of the landmarks on the frontal and lateral images

Statistical analyses

Statistical analyses were performed using the PASW software package (version 18, SPSS, Chicago). Intraobserver and interobserver reliability were investigated by determining relative and absolute reliability.[10] Relative and absolute intraobserver reliability were investigated by respectively

calculating intraclass correlation coefficients (ICCs) and using the Bland & Altman method.[10] The ICCs with 95% confidence interval (CI) for each 2D and 3D measurement were calculated and interpreted according to the benchmarks described by Fleiss. An ICC >0.75 represents an excellent correlation, 0.400.75 a moderate-to-good correlation and <0.40 represents a poor correlation.[11]

Absolute intraobserver and interobserver reliability were calculated by the Bland & Altman method.[12] For intraobserver reliability the mean difference and 95% CI between measurement set 1 (M1) and measurement set 2 (M2) were calculated for both observers separately. For interobserver reliability the mean difference and 95% CI between the two observers were calculated. When intraobserver reliability was good for both observers, the means of M1 and M2 of observer A (n=40) were compared with the means of both sets of observer B (n=40).

To investigate agreement on the number of outliers between M1 and M2, as well as the two observers, Cohen's kappa coefficients were calculated.[13] Angles with a deviation >3˚ varus or valgus from the neutral axis were considered outliers.[6] The values were interpreted according to Landis and Koch[14]: <0 represents less than chance agreement, 0.010.20 represents slight agreement, 0.210.40 fair agreement, 0.410.60 moderate agreement, 0.610.80 substantial agreement and 0.810.99 represents almost perfect agreement. ^{2} tests were performed to assess statistically significant differences in the number of outliers.

To identify significant differences between M1 and M2, a paired Student T-test was performed and the standard error of measurement (SEM) and smallest detectable change (SDC) were calculated. The formulas used to calculate the SEM and SDC are respectively SEM = standard error of difference / √2 and SDC = 1.96 x √2 x SEM.[15-17] A Student T-test for independent samples was performed to assess significant differences between the means of the measurements of the two observers, and the SEM and SDC were calculated.

Potential differences between VV2D and VV3D measurements were assessed using T-tests. First, the means of M1 and M2 of each observer for

both VV2D and VV3D were calculated, creating a VV2D and VV3D set (n=40/n=40) for each observer. Next, the means of the mean of observer A and observer B for both VV2D and VV3D were calculated. In this way, one set of VV2D and one set of VV3D measurements was generated (n=40/n=40). A Paired-samples T-test was performed to detect any significant differences between both sets. The absolute difference between VV2D and VV3D was calculated for each subject. Meaning, the deviation of the neutral axis was stated as a positive value, regardless of the deviation being varus or valgus. The absolute differences were compared with the value 0 using a One-sample T-test, since a zero value indicates no absolute difference between VV2D and VV3D. Additionally, Cohen's kappa was calculated to determine agreement on the number of outliers between measurements of VV2D and VV3D, with an outlier defined as >3˚ varus or valgus. A chi-square test was performed to assess statistically significant differences in the number of outliers between VV2D and VV3D. For all statistical analyses, a p-value of <.05 was considered to indicate statistical significance.

Results

On 14 of the 54 images it was not possible to identify medial and lateral condyles of the femoral component on the LAT X-ray and were excluded from further analysis. Eventually, 40 AP and LAT images were available for final analysis. The patient population consisted of 21 men and 16 women, with a mean age of 64.5 years (range 3283). Of the 40 sets of images, 23 images were made of the left lower limb and 17 of the right lower limb.

Relative intraobserver reliability was excellent when measuring VV2D and VV3D, with ICCs ≥0.98 (Table 1). There was no significant difference between the means of M1 and M2 for any angles. Absolute intraobserver reliability showed no significant bias between for VV2D and VV3D. The SEM was 0.20˚ and the SDC 0.55˚ for VV2D. For VV3D, the SEM was 0.43˚ and the SDC 1.20˚. The calculated kappa coefficient was 0.94 for both VV2D and VV3D.

Relative interobserver reliability was excellent for both angles, with ICCs ≥0.96 (Table 1). There was no significant difference between the

measurements of observer A and observer B. Absolute interobserver reliability of VV2D and VV3D showed no significant bias between the measurements of the two observers. The SEM was 0.41˚ and the SDC 1.14˚ for VV2D. For VV3D, the SEM was 0.64˚ with an SDC of 1.77˚. The kappa coefficient was 0.78 for VV2D and 0.88 for VV3D.

There was a significant mean and absolute difference between VV2D and VV3D measurements. The mean difference between VV2D and VV3D was 1.00˚ (1.660.34) (p=0.004) and the mean absolute difference was 1.61˚ (1.092.13), with a p-value of <0.001 (Table 2). The kappa coefficient for the agreement between the outliers as determined on 2D and 3D was 0.50.

Scatter graphs of the Bland & Altman method and tables of the distribution of outliers are presented in the Appendix.

Table 1. Reported intraobserver and interobserver reliability of varus/valgus angle measured in 2D and 3D

*Results are given as mean (sd). Abbreviations: VV2D: varus/valgus angle in 2D,

Intraobserver reliability									
	M1*	M2*	Difference M1-M2 (95% CI)	Range of difference M1-M2	P-value	ICC (95% CI)	SDΔ	SEM	SDC
VV2D	-1.0 (3.7)	-1.0 (3.8)	-0.02 (-0.11, 0.07)	-0.7, 0.6	0.66	1.00 (1.00, 1.00)	0.28	0.20	0.55
VV3D	-1.9 (3.2)	-2.0 (3.4)	0.08 (-0.11, 0.28)	-1.3, 2.7	0.39	0.98 (0.97, 0.99)	0.61	0.43	1.20
Interobserver reliability									
	Obs. A*	Obs. B*	Difference Obs. A-B (95% CI)	Range of difference obs. A-B	P-value	ICC (95% CI)	SDΔ	SEM	SDC
VV2D	-1.1 (3.8)	-0.9 (3.7)	-0.16 (-0.34, 0.03)	-1.5, 0.8	0.85	0.99 (0.98, 0.99)	0.58	0.41	1.14
VV3D	-2.0 (3.4)	-1.9 (3.2)	-0.10 (-0.39, 0.19)	-2.5, 2.2	0.90	0.96 (0.93, 0.98)	0.91	0.64	1.77

VV3D: varus/valgus angle in 3D, M1: measurement session 1, M2: measurement session 2, sd: standard deviation, CI: confidence interval, ICC: intraclass correlation coefficient, SDΔ: standard error of difference, SEM: standard error of measurement, SDC: smallest detectable change, Obs.: observer. Angles are expressed in degrees (˚).

Table 2: Difference between 2D and 3D varus/valgus angle measurements

	Mean	SD	Mean difference	95% CI	P-value
VV2D	-.98	3.75	1.00	1.66 – 0.34	0.004
VV3D	-1.97	3.28			
Diff	1.61	1.62		1.09 – 2.13	<0.001

Abbreviations: VV2D: varus/valgus angle in 2D, VV3D: varus/valgus angle in 3D, sd: standard deviation, CI: confidence interval, SDΔ: standard error of difference, SEM: standard error of measurement, SDC: smallest detectable change. Results are given as mean (sd). Angles are expressed in degrees (°).

DISCUSSION

A new low-dose X-ray device, called EOS, was recently introduced for determining lower-limb alignment in 2D and 3D.[7] Reliability has not yet been assessed when performing EOS measurements on lower limbs containing a knee prosthesis. Purpose of this study was to determine intraobserver and interobserver reliability of 2D and 3D knee prosthesis alignment measurements after rTKA. Potential differences between 2D and 3D measurements were assessed as a secondary outcome.

Intraobserver and interobserver reliability were excellent for VV2D and VV3D, with no significant differences or systematic bias between the measurements of the two measurement sessions or observers. SEM and SDC of both VV2D and VV3D were small, but larger for VV3D. The coefficients showed substantial to almost-perfect intraobserver and interobserver reliability for determining outliers, for both 2D and 3D measurements. A significant mean and absolute difference existed between the angles measured in 2D and 3D.

Results of this study are comparable to other studies investigating reliability of EOS. Intraobserver and interobserver reliability were excellent when measuring VV2D and VV3D (with ICCs >0.99) on lower limbs containing no knee prostheses.[18] Interobserver reliability was good for EOS 3D varus/valgus measurements on lower limbs of children containing no knee prostheses (Pearson correlation coefficient (Pr) 0.82).[19] Reliability studies on

measurements of vertebrae,[20] sagittal balance and spine curves (Pr ≥0.85 and ICCs ≥0.85),[21] spinal curve measurements (ICCs ≥0.84),[22] scoliosis (ICCs ≥0.97),[23] shoulder bony landmarks,[24] pelvic and acetabular morphology (ICCs ≥0.80),[25] and pelvic tilt and acetabular cup orientation (ICCs 0.690.98),[26] also showed good overall reliability.

SEM and SDC for VV3D were greater than VV2D for both intraobserver and interobserver reliability. A smaller SEM and SDC means that measurements are more precise, but that doesn't indicate which of the two measurement types is more accurate or valid. In this study the SEM and SDC were larger for VV3D than for VV2D. This can be explained by the way in which 2D and 3D measurements are calculated. Since a 3D measurement is calculated through a combination of two planes (coronal and sagittal) and a 2D measurement is measured in the coronal plane only, slightly more variation can be expected in the 3D measurements and thus a higher SEM and SDC.

One could debate whether the significant differences between 2D and 3D measurements are of clinical importance. Both the mean and absolute difference were small (1.00˚ (1.660.34) and 1.61˚ (1.092.13), respectively). The mean difference is smaller than the absolute difference. For the absolute difference, we stated the deviation of the neutral axis as a positive value, regardless of the deviation being varus or valgus. For the mean difference, varus was stated as a negative value and valgus as a positive value. Calculating the mean difference using both positive and negative values, the deviation may be underestimated. There was only a moderate agreement between 2D and 3D measurements for assessment of outliers — meaning that in 2D different lower limbs are defined as outliers than in 3D.

The influence of lower-limb positioning on 2D measurements has been shown in previous studies. Varus or valgus deformity, axial rotation and flexion of the lower limb at the time of assessment of the radiographs alter coronal measurements of knee alignment.[27-30] When a measurement is taken in 3D, the system mathematically corrects for potential malpositioning during acquisition. EOS VV3D measurements of legs that not contain a knee

prosthesis are more accurate than VV2D measurements, eliminating bias due to wrong lower-limb positioning.[31] Validity of EOS VV3D on legs not containing prosthetic material was also investigated in a cadaveric study[19] that measured varus/valgus angle three times using CT-scanning and EOS 3D with each specimen in three different positions: neutral, 10˚ external rotation and 10˚ internal rotation. No significant differences between CT and EOS 3D measurements were observed. To gain more insight into validity, additional research has to be conducted in which the accuracy of VV2D and VV3D EOS measurements on lower limbs containing a knee prosthesis are investigated.

This study has some limitations. First of all, when generating a 3D reconstruction of the lower limb with the EOS software it is possible to use the full 3D mode or the lower-limb alignment mode. When using the full 3D mode more angles can be calculated for knee prosthesis alignment, but even more landmarks that have disappeared or changed have to be identified. Hence it was decided not to use the full 3D mode because of a greater chance of errors. Secondly, when it was not possible to identify the medial and lateral condyles on the lateral images, the patient was excluded. In order to identify them on both the AP and the LAT image the condyles have to differ in height on the EOS images. To prevent this in the future, whether the condyles differ in height has to be checked directly after acquisition, otherwise acquisition has to be repeated. Finally, no generally accepted measurement protocol exists for 3D reconstructions of limbs with knee prosthesis material *in situ*. To tackle this issue, the two observers drew up a measurement protocol.

Our study showed that EOS provides reliable varus/valgus measurements of lower limbs containing a revision knee prosthesis in 2D and 3D. There is however a significant difference between varus/valgus measurements in 2D and 3D.

CONFLICT OF INTEREST

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Chapter 5

The validity of a new low-dose stereoradiography system to perform 2D and 3D knee prosthetic alignment measurements

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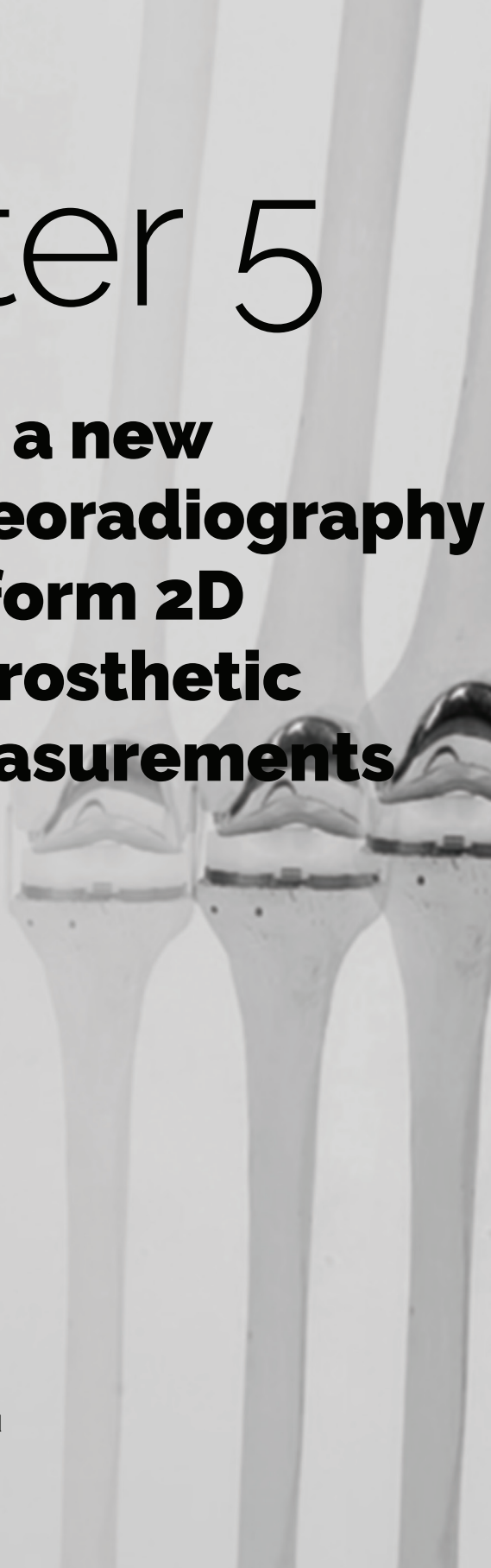

Submitted

ABSTRACT

Introduction: The EOS stereoradiography system has shown to provide reliable varus/valgus (VV) measurements in 2D (VV2D) and 3D (VV3D) after total knee arthroplasty (TKA). Validity of these measurements has not been investigated yet, therefore the purpose of this study was to determine validity of EOS VV2D and VV3D.

Methods: EOS images were made of an artificial leg containing a knee prosthesis, while varying VV angle from 15˚ varus to 15˚ valgus and flexion angle from 0˚ to 20˚, and changing rotation from 20˚ internal to 20˚ external rotation. Differences between the actual VV position of the artificial leg and its position as measured on EOS 2D and 3D images were investigated.

Results: Rotation, flexion or VV angle alone had no major impact on VV2D or VV3D. Combination of VV angle and rotation with full extension did not show major differences in VV2D measurements either. Combination of flexion and rotation with a neutral VV angle showed variation of up to 7.4˚ for VV2D; maximum variation for VV3D was only 1.5˚. A combination of the three variables showed an even greater distortion of VV2D, while VV3D stayed relatively constant. Maximum measurement difference between preset VV angle and VV2D was 9.8˚, while the difference with VV3D was only 1.9˚. The largest differences between the preset VV angle and VV2D were found when installing the leg in extreme angles, for example 15˚ valgus, 20˚ flexion and 20˚ internal rotation.

Conclusions: After TKA, EOS VV3D were more valid than VV2D, indicating that 3D measurements compensate for malpositioning during acquisition. Caution is warranted when measuring VV angle on a conventional radiograph of a knee with a flexion contracture, varus or valgus angle and/or rotation of the knee joint during acquisition.

INTRODUCTION

Achieving optimal prosthetic alignment during total knee arthroplasty (TKA) is crucial, as malalignment is associated with worse functional outcome, earlier aseptic loosening of the prosthesis and, eventually, revision surgery (rTKA).[1-6]

Long leg standing radiographs (LLRs) are frequently used to measure knee prosthesis alignment in the coronal plane. Assessment of alignment with LLRs in the sagittal plane is not common practice, and mostly lateral radiographs of the knee are used. With LLR this 2D measurement technique has some pitfalls though. Due to divergence in the horizontal and vertical planes, measured angles may not be correct. More importantly, validity of the measurements is easily influenced by the position of the patient's lower limb during acquisition. Varus or valgus angle, rotation and flexion of the lower limb are shown to influence alignment measurements.[7-10]

To tackle this issue, 3D measurements such as CT-scanning have been developed to perform these measurements, but major drawbacks of this technique are the costs and high doses of radiation. Furthermore, CT-scanning is done in non-weight bearing position. The EOS system (EOS Imaging, Paris, France)[11] is a new alternative: its 3D measurements of this system are based on two orthogonally made LLRs done on a 1:1 scale. This system uses an even lower dose of radiation than normal X-rays.[11,12] Since the leg is scanned by a C-arm that moves up and down while the patient is standing, divergence in the vertical plane is diminished and images are weight bearing.

The EOS system uses sterEOS software (EOS Imaging, Paris, France) to create EOS 3D reconstructions of the LLRs made. This software is originally designed for lower limbs not containing a knee prosthesis. We have developed a protocol to perform 3D varus/valgus (VV3D) measurements on patients with a knee prosthesis, and concluded that this measurement protocol has excellent intra- and interobserver reliability.[13] In this study, significant differences between EOS 2D varus/valgus (VV2D)

and VV3D measurements were found. It was hypothesized that the 2D measurement might be influenced by malpositioning during acquisition while the 3D measurement mathematically corrects for this issue, but validity of this 3D measurement protocol for lower limbs containing a knee prosthesis has not been investigated yet.

Hence the aim of this study was to investigate the validity of EOS VV2D and VV3D measurements in a lower limb containing a knee prosthesis. As no gold standard for performing knee prosthesis alignment measurements exists, we designed a phantom study using an artificial lower limb containing a knee prosthesis in which we could alter varus/valgus (VV), flexion and rotation of the lower limb while obtaining EOS images.

MATERIALS AND METHODS

An artificial left lower limb (Sawbones® Inc., Vashon Island, WA, USA) containing a NexGen Legacy Posterior Stabilized Knee® prosthesis was used. The lower limb was fixed into a frame in which it was possible to change VV and flexion/extension angle by moving the femur. The distal tibia was fixed to the base plate (Fig. 1). An extendable goniometer was used to set the lower limb in different varus/valgus and flexion/extension positions. The protractor at the base of the construction was used to place the construction in different angles of rotation during acquisition.

VV was varied from 15˚ varus to 15˚ valgus with 5˚ increments. A negative value (-) indicated varus and a positive value (+) indicated valgus. Flexion was varied from 0˚ to 20˚ with 5˚ increments. Rotation was varied from 20˚ internal rotation to 20˚ external rotation. A negative value (-) indicated internal rotation and a positive value (+) indicated external rotation. The influence of these three variations in lower-limb position on EOS VV2D and VV3D measurements were investigated both separately and combined. Settings of the EOS system during acquisition of the images was scan speed 2 (6 in/s), voltage 55 kV and amperage 32 mA.

All EOS VV2D and VV3D measurements were performed by a radiology assistant (TV) who had extensive experience in taking such measurements and who was blinded to the preset lower limb-positions. SterEOS software (EOS Imaging, Paris, France) was used to perform VV2D measurements on the anterior-posterior (AP) image and VV3D measurements on the AP and lateral (LAT) images. The measurement protocol that was used is described extensively in our previous publication.[13]

In order to calculate coronal and sagittal alignment parameters of the lower limb in 2D and 3D, the 'lower limb alignment' mode was used. The first step was to define the left or right lower limb and to choose the modeling 'lower limb alignment' mode. Next, identification of the lower limb on the AP and LAT images was done in 10 steps (Fig. 2):

Femur:

- center of the femoral head (points 1 and 4);
- center of the distal femoral notch (points 2 and 5);
- center of the diaphysis in its distal third (points 3 and 6).

Tibia:

- center of the tibial plateau. the axis from the center of the ankle to the center of the tibial plateau represents the anatomical axis of the tibia (points 7 and 9);
- center of the distal articular surface in the upper ankle joint (points 8 and 10).

The next step was adjustment of the landmarks in four steps (Fig. 3):

1. Adjustment of the position of the sphere of the femoral head in both views. It is possible to enlarge or minimize the size of the sphere according to the size and shape of the femoral head, in order to mark the center of the femoral head as precisely as possible;
2. Adjustment of the point in the center of the distal third of the femoral diaphysis;

3. Adjustment of the position of the point in the center of the femoral notch and tibial plateau, and marking of the femoral condyles. The condyles have to be identified on the AP and LAT images using the two spheres. It is possible to adjust the size of the spheres according to the size of the condyles. On the AP image the center of the spheres has to be located in the center of each condyle. On the LAT image the spheres have to be tangent to the posterior part of the condyles. It is important not to confuse the medial with the lateral condyles. In order to identify the right condyle, the epipolar line is used to differentiate between the two condyles by observing the correspondence of condylar height on both the AP and the LAT image;
4. Adjustment of the reference point in the center of the distal articular surface on the AP and LAT images.

VV2D is the angle between the mechanical axis of the femur (axis between points 1 and 2) and the tibia (axis between points 7 and 8) on the AP image (Fig. 2). For the 3D measurement, the points marked on the AP and LAT (Fig. 2) images as described above are combined to generate the mechanical axes of the femur and tibia. VV3D is the angle between the three-dimensional mechanical axis of the femur (axis between points 1-4 and 2-5) and tibia (axis between point 7-9 and 8-10).

Statistical analyses

All statistical analyses were performed using the IBM SPSS Statistics for Windows software (Version 22.0, IBM Corp., Armonk, NY, USA). Intraobserver reliability of setup installation was investigated. To that end, seven different combinations of VV, flexion and rotation were installed twice. VV angle of the first setup was compared to the second setup for both 2D and 3D. Relative intraobserver reliability of the setup was investigated by calculating the Intraclass Correlation Coefficients (ICCs).[14] ICCs were interpreted according to the benchmarks described by Fleiss[15]:

Figure 1 (left). The experimental setup.

Figure 2 (right). Identification of the landmarks on the frontal and lateral images.

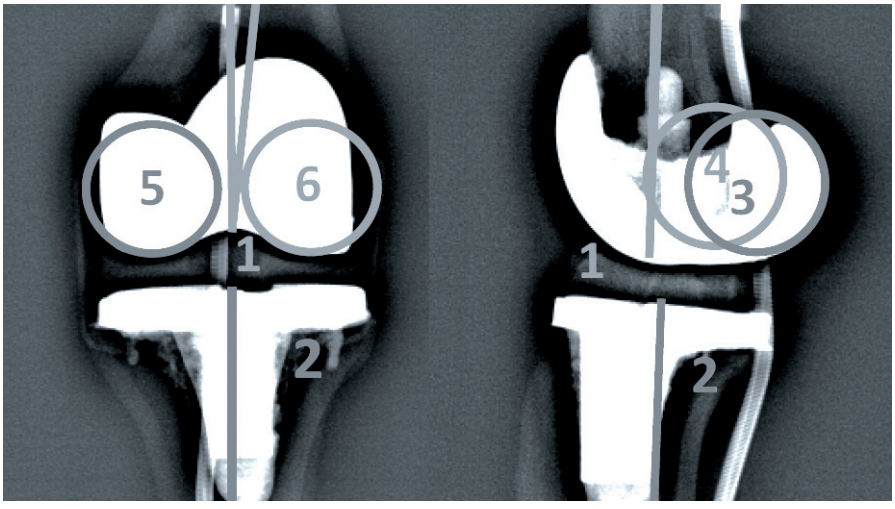

Figure 3. Adjustment of the landmarks on the frontal and lateral images.

an ICC >0.75 represents an excellent correlation, 0.40-0.75 moderate-to-good and <0.40 represents a poor correlation.[15] The Bland & Altman method was used to investigate absolute intraobserver reliability of the setup.[16] Mean difference and 95% confidence interval (CI) between measurements 1 and 2 were calculated. When zero lies in the 95% CI, no systematic bias exists between the measurements.

To compare the VV2D and VV3D for different positions of the artificial lower limb, the mean absolute differences and range of the absolute differences were used. Mean difference was not calculated, as varus and valgus are negative and positive values respectively, thus calculating the mean leads to an underestimation of the differences. On the other hand, the range of the absolute differences might give an underestimation of the effect, due to elimination of varus or valgus direction. For this reason, besides the range of the absolute differences we also showed the original range.

RESULTS

Relative intraobserver reliability for setup installation was excellent, with an ICC of 0.98 (95% CI: 0.94 – 1.00) for both VV2D and VV3D. Absolute intraobserver reliability did not show a systematic bias for either VV2D (95% CI: 1.51 – 0.15) or VV3D (95% CI: 2.12 – 0.02) (Appendix).

The results of the influence of the preset VV and flexion angles alone and combined on the VV2D and VV3D are shown in Table 1. When the leg was positioned in 0˚ VV and 0˚ flexion and the construction was rotated from 20˚ to 20˚ with 5˚ increments, the mean absolute difference between the preset VV angle and VV2D was 0.73˚ (SD: 0.49; range: 0.1˚ – 1.5˚) and the mean absolute difference between the preset VV angle and VV3D was 0.79˚ (SD: 0.51; range: 0.2˚ – 1.5˚) (Table 1, Fig 4A). When the leg was positioned in 0˚ VV and 0˚ rotation while varying the flexion angle from 0˚ to 20˚ with 5˚ increments, the mean absolute difference between the preset VV angle and VV2D was 1.02˚ (SD: 0.27; range: 0.6˚ – 1.2˚) and the mean absolute difference between the preset VV angle and VV3D was 1.22˚ (SD: 1.04; range: 0.3˚ – 2.9˚) (Fig 4B). When the leg was positioned in 0˚ flexion and rotation while varying the VV from 15˚ varus to 15˚ valgus

with 5˚ increments, the mean absolute difference between the preset VV angle and the VV2D was 1.09˚ (SD: 0.51; range 0.5˚ – 1.7˚) and the mean absolute difference between the preset VV angle and VV3D was 1.01˚ (SD: 0.58; range: 0.0˚ – 1.5˚) (Fig 4C).

Three different combinations of VV and flexion angles are shown in Figure 5. Scatter dots of other combinations of VV and flexion angles are added in the Appendix.

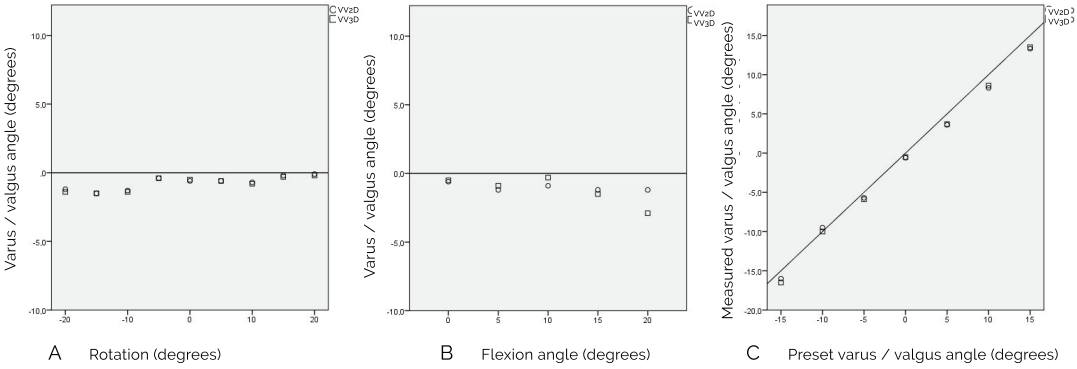

Figure 4: The influence of rotation, flexion and varus/valgus angle on EOS 2D and 3D varus/valgus measurements. A: The preset varus/valgus and flexion angles were 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments. B: The preset varus/valgus angle and rotation were 0˚ and the flexion angle was varied from 0˚ to 20˚ with 5˚ increments. C: The preset flexion angle and rotation were 0˚ and the varus/valgus angle was varied from 15˚ varus to 15˚ valgus with 5˚ increments.

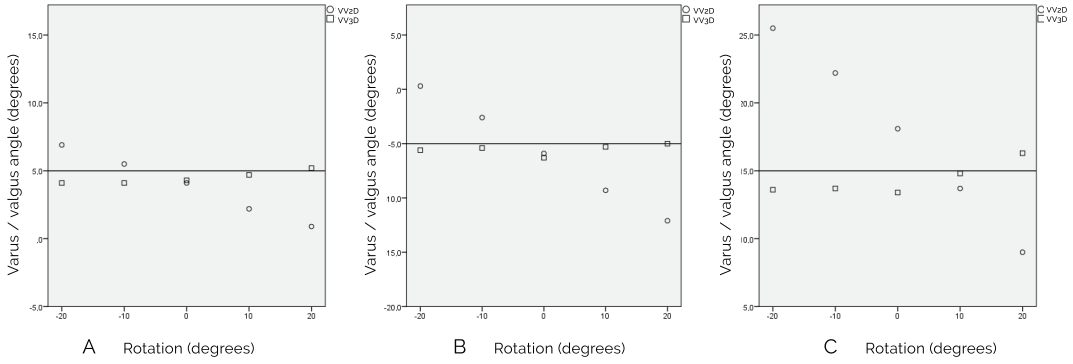

Figure 5: EOS 2D/3D measurements of varus/valgus angle for different combinations of preset varus/valgus and flexion angle and rotation. A: The preset angles were 5˚ valgus and 10˚ flexion. B: The preset angles were 5˚ varus and 20˚ flexion. C: The preset angles were 15˚ valgus and 20˚ flexion.

Table 1. Results of the measured varus/valgus angles in 2D and 3D for different positions.

Varus/valgus	Flexion	Mean abs diff 2D (SD)	Range abs diff 2D	Range diff 2D	Mean abs diff 3D (SD)	Range abs diff 3D	Range diff 3D
0	0	0.73 (0.49)	0.1–1.5	0.1–1.5	0.79(0.51)	0.2–1.5	0.2–1.5
5	0	1.62 (0.15)	1.4–1.8	1.4–1.8	1.38(0.28)	1.0–1.7	1.0–1.7
-5	0	0.62 (0.13)	0.4–0.7	0.4–0.7	1.14(0.63)	0.7–2.2	0.7–2.2
10	0	1.82 (0.26)	1.6–2.1	1.6–2.1	1.28(0.65)	0.3–1.9	0.3–0.9
-10	0	0.72 (0.57)	0.3–1.7	-1.7 – -0.3	0.46(0.30)	0.0–0.7	-0.7–0.7
15	0	2.14 (0.49)	1.7–2.9	1.7–2.9	1.40(0.54)	0.7–1.9	0.7–1.9
-15	0	0.64 (0.39)	0.1–1.0	-0.1–1.0	1.56(0.49)	1.0–2.2	1.0–2.2
0	10	2.2 (1.38)	0.9–4.2	-2.3–4.2	0.5(0.25)	0.3–0.9	0.3–0.9
0	20	4.54 (2.88)	1.2–8.6	-5.2–8.6	2.42(0.65)	1.8–3.3	1.8–3.3
5	10	2.04 (1.46)	0.5–4.1	-1.9–4.1	0.60(0.33)	0.2–0.9	-0.2–0.9
5	20	3.92 (2.23)	1.4–6.8	-6.8–5.3	0.96(1.15)	0.3–3.0	-3.0–0.4
10	10	2.2 (1.43)	0.1–4.0	-2.9–4.0	0.32(0.29)	0.1–0.8	-0.1–0.8
10	20	4.52 (2.61)	1.7–8.2	-8.2–5.6	1.06(0.85)	0.0–2.3	-2.3-0
15	10	2.62 (1.22)	1.3–4.2	-3.2–4.2	0.50(0.34)	0.0–0.9	-0.9–0.7
15	20	5.6 (3.59)	1.3–10.5	-10.5–6	1.16(0.55)	0.2–1.6	-1.3–1.6
-5	10	2.24 (1.61)	0.2–4.4	-1.8–4.4	0.84(0.21)	0.6–1.1	0.6–1.1
-5	20	4.00 (2.43)	0.9–7.1	-5.3–7.1	0.52(0.49)	0.0–1.3	0.0–1.3
-10	10	2.42 (1.84)	0.0–4.9	-2.0–4.9	2.84(0.78)	1.8–3.8	1.8–3.8
-10	20	3.68 (2.24)	0.6–6.2	-6.2–5.5	2.06(0.38)	1.5–2.5	-2.5 – -1.5
-15	10	2.50 (1.63)	0.7–4.9	-4.9–3.1	0.46(0.26)	0.2–0.8	-0.8 – -0.2
-15	20	5.00 (3.72)	0.8–10.6	-4.4–10.6	2.18(0.72)	1.1–3.0	1.1–3.0

The synthetic leg was positioned in a preset varus/valgus and flexion angle, while rotation of the construction was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments. Angles are expressed in degrees (˚). Abbreviations: Mean abs diff 2D = mean absolute difference between preset varus/valgus angle and varus/valgus angle measured in 2D; SD = standard deviation; Range abs diff 2D = range of absolute difference between preset varus/valgus angle and varus/valgus angle measured in 2D; Range diff 2D = range of difference between preset varus/valgus angle and varus/valgus angle measured in 2D; Mean abs diff 3D = mean absolute difference between preset varus/valgus angle and varus/valgus angle measured in 3D; Range abs diff 3D = range of absolute difference between preset varus/valgus angle and varus/valgus angle measured in 3D; Range diff 3D = range of difference between preset varus/valgus angle and varus/valgus angle measured in 3D.

DISCUSSION

With the EOS system it is possible to measure knee prosthesis alignment measurements in 2D and 3D. Intra- and interobserver reliability for measuring VV angle in 2D and 3D after TKA are shown to be excellent,[13] but validity has not been investigated yet. Previous research demonstrated that

significant differences exist between EOS VV2D and VV3D measurements.[13] It was hypothesized that VV angle and malpositioning during acquisition influenced 2D measurements, but not 3D measurements. Aim of this study was therefore to study the validity of EOS 2D and 3D VV measurements using an artificial lower limb containing a knee prosthesis.

Our results showed that validity of VV3D is good, but VV2D showed considerable variation. Rotation, flexion or VV angle alone did not have a major impact on VV2D or VV3D. The combination of VV angle and rotation in full extension did not show major differences in VV2D or VV3D measurements either. The combination of flexion and rotation with a neutral VV angle showed variation of up to 13.8° for VV2D, while maximum variation for VV3D was only 1.5°. A combination of the three variables demonstrated an even greater variety. Maximum measurement difference of VV2D was 16.5°, while VV3D differed only 2.9° in that same setup. The largest differences between the preset VV angle and the VV2D measurement error were found with the leg in extreme positions, for example 15° valgus, 20° flexion and 20° internal rotation.

To our knowledge, no studies have been conducted in which an artificial leg containing a knee prosthesis was used to investigate the influence of VV angle and/or malpositioning on VV measurements. There are however studies in which an artificial lower limb containing no prosthetic material was used. Radtke et al.[9] reported on the influence of rotation (-20° - 20°) on the VV measurements on conventional AP radiographs. The artificial leg used was set at 6.5° valgus. The measured VV angle varied from 4.6° to 6.8° valgus. This is in line with our conclusion that a VV angle in combination with rotation does not cause large variations in VV2D. Lonner et al.[7] found that the combination of 5° valgus, 10° flexion and rotation varying from 25° internal to 20° external rotation caused a significant difference of 4.4° between preset VV angle and VV2D. We used a similar setup but a maximum internal rotation of 20° and found a difference of 6.0° between preset VV angle and VV2D, which is comparable to the results of Lonner et al.[7] Swanson et al.[10] concluded that VV2D is more sensitive to rotation in combination with VV angle; in their study, the anatomical

axis of the artificial leg was set at 18˚ valgus and 0˚ flexion. When rotating from 10˚ internal rotation to 20˚ external rotation the measured anatomical angle in 2D ranged from 20.2˚ to 13.6˚ valgus respectively. In our study the effect was not as outspoken. When we set the artificial leg at a mechanical axis of 15˚ valgus and 0˚ flexion, the maximum difference between the preset VV angle and the VV2D was 2.9˚; at a mechanical axis of 15˚ varus and 0˚ flexion the maximum difference between the preset VV angle and the VV2D was 1.0˚. Brouwer et al.[8] investigated the influence of flexion and rotation alone and in combination on the VV angle measured on conventional X-rays. The cadaveric leg used in their study had a VV angle of 10˚ varus. They found that flexion of the knee (from 0˚ to 30˚) or rotation of the lower limb (from -30˚ - 30˚) separately had very little effect on the angles measured on the AP radiograph. Simultaneous flexion and rotation, however, caused large changes (up to 28˚) in the measured VV angle. This is in line with the results of our study. A combination of VV angle with flexion alone did not show great variety in the VV2D in our study either, but when rotation was added VV2D varied significantly.

Differences between VV2D and VV3D EOS measurements have been reported previously. Thelen et al.[17] conducted a phantom study with an artificial lower limb without a knee prosthesis to investigate the influence of flexion and rotation in VV2D and VV3D. The preset VV angle of the lower limb was 5˚ valgus. They found that the combination of 5˚ valgus, flexion (up to 18˚) and rotation provoked VV2D measurement errors up to 6.8˚, compared to 1.5˚ for VV3D. Their conclusion was that 3D modeling allows for more valid evaluation of coronal alignment than 2D, eliminating bias due to an abnormal knee positioning. The original SterEOS measurement protocol, as also used in the study of Thelen et al.,[17] is designed for lower limbs not containing a knee prosthesis. Since no official measurement protocol existed for performing these measurements after TKA, we drew up a measurement protocol,[13] and validity of that protocol is investigated in this study. We also wanted to evaluate the influence of VV angle on VV2D and VV3D further, and varied this angle from 15˚ varus to 15˚ valgus. No previous studies with or without knee prosthesis in situ have investigated

the influence of 15˚ varus or valgus on the effect on VV2D measurements. Thelen et al.[17] fixed their phantom at 5˚ valgus. We added the extreme positions of 15˚ varus to 15˚ valgus to the analyses, as these deformities do occur in clinical practice. Results of our study are comparable to those of Thelen et al.[17]: we also concluded that VV3D measurements are more valid than VV2D measurements, since VV3D corrects for malpositioning during acquisition while VV2D does not.

This study has some limitations. First of all, the study was conducted with use of an artificial lower limb, therefore the EOS images differed from those obtained from patients. Still, with adjustment of the scan speed, voltage and amperage settings we were able to get good visualization of the bony structures. Secondly, it was not possible to compare validity of the EOS system to a gold standard, as there isn't one for measuring VV angle. We therefore designed this experimental setup using an artificial leg and an extendable goniometer. Despite not having a gold standard, installing the artificial leg showed excellent intraobserver reliability, the influence of malpositioning and angle on 2D measurements was clear, and 3D measurements stayed relatively constant.

To our knowledge, this is the first study to investigate validity of EOS VV2D and VV3D measurements in a leg containing a knee prosthesis. Our study showed that EOS VV3D measurements are more valid than EOS VV2D measurements, since VV2D measurements are influenced by VV angle and malpositioning. A combination of flexion and rotation caused major variation in VV2D measurements. A combination of varus or valgus angle, flexion and rotation caused an even larger variation in VV2D measurements.

In clinical practice a combination of flexion deformity and VV deformity frequently meet, and one should pay extra attention when positioning the patient so as to obtain an LLR without adding a rotation error. Orthopedic surgeons should also be aware of this phenomenon, and caution is warranted when measuring VV angle on a conventional radiograph when the patient has a knee with a flexion contracture,

varus or valgus angle and/or is standing with a rotated knee joint during acquisition. Hence it can be concluded that EOS 3D reconstructions are a valid and reliable method for measuring varus/valgus angle after TKA. EOS 3D reconstructions are superior to conventional anteroposterior LLRs, as EOS 3D measurements will be corrected for unseen deformities and malpositioning.

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CONFLICT OF INTEREST

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Chapter 6

Do CAS measurements correlate with EOS 3D alignment measurements in primary TKA?

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ABSTRACT

Purpose: Objective of this study was to compare intraoperative computer-assisted surgery (CAS) alignment measurements during total knee arthroplasty (TKA) with pre- and postoperative coronal alignment measurements using EOS 3D reconstructions.

Methods: In a prospective study 56 TKAs using imageless CAS were performed and coronal alignment measurements were recorded twice: before bone cuts were made and after implantation of the prosthesis. Pre- and postoperative coronal alignment measurements were performed using EOS 3D reconstructions. With the EOS radiostereography system, measurement errors due to malpositioning and deformity during acquisition are eliminated. CAS measurements were compared with EOS 3D reconstructions. Measured were varus/valgus angle (VV), mechanical lateral distal femoral angle (mLDFA) and mechanical medial proximal tibial angle (mMPTA).

Results: Significantly different VV angles were measured pre- and postoperatively with CAS compared to EOS. For preoperative measurements mLDFA did not differ significantly, but a significantly larger mMPTA in valgus was measured with CAS.

Conclusions: Results of this study indicate that differences in alignment measurements between CAS measurements and pre- and postoperative EOS 3D are mainly due to the difference between weight bearing and non-weight bearing position and potential errors in validity and reliability of the CAS system. EOS 3D measurements overestimate VV angle in lower limbs with substantial mechanical axis deviation. For lower limbs with minor mechanical axis deviation as well as for mMPTA measurements, CAS measures more valgus than EOS. Surgeons should be aware of these measurement differences and the pitfalls of both measurement techniques.

INTRODUCTION

Total knee arthroplasty (TKA) is a successful surgical treatment for end-stage osteoarthritis. To achieve good short- and long-term results, optimal knee prosthesis alignment is crucial. Malalignment in TKA leads to increased wear and a higher risk of aseptic loosening, resulting in revision TKA (rTKA).[1-4] Moreover, malaligned prostheses are associated with inferior clinical results and longer hospital stay.[5-7] Assessing alignment intraoperatively is possible using computer-assisted surgery (CAS). There are several techniques to assess alignment pre- and postoperatively.

Goal during TKA is to achieve a neutral mechanical leg axis and to place the femoral and tibial component in neutral alignment.[7-9] CAS has been developed to improve knee prosthesis alignment and to reduce the number of outliers; multiple studies have shown significant improvement over conventional techniques.[10-16] The use of CAS during TKA (CAS-TKA) also gives a surgeon the possibility to perform reliable intraoperative lower limb alignment measurements.[17-20]

Lower limb alignment measurements are important for both preoperative planning and postoperative evaluation of TKA. Several methods for coronal alignment measurement exist. Long-leg standing radiographs (LLR) are mostly used in clinical practice to assess coronal alignment pre- and postoperatively. Advantages of this technique are the availability in most centres, low radiation dose and weight bearing images. A disadvantage is the divergence in both the horizontal and vertical planes, which affects the validity of the measurements. Moreover, varus and valgus deformity, rotation and flexion of the leg during acquisition are known to influence coronal alignment measurements, making measurements less valid.[21-24] One could also use CT-scan to overcome these problems, but that technique involves a higher level of radiation, is more costly, and produces non-weight bearing images.

Several studies have compared intraoperative imageless CAS measurements with pre- and postoperative LLR measurements.[25-29] Willcox et al.[26] showed that there are discrepancies between intraoperative

CAS measurements and those performed on LLRs. The radiological measurements tended to show a larger deformity than CAS measurements. Babazadeh et al.[25] compared alignment measurements of LLR, CT-scan and CAS. They found that measurements of LLRs and CT were well-correlated, but little agreement existed between CAS measurements and the two modalities. Reasons for this could be that the CAS measurements are non-weight bearing, the capsule is unclosed, and the system itself is subject to observer error.[25,26] Discrepancies between CAS and LLR measurements can also be based on the variability of alignment measurements due to limb malpositioning during acquisition of LLR. Yaffe et al.[28] found a greater discrepancy between CAS and LLR measurements with larger lower limb deformities. Varus or valgus deformity in combination with malpositioning during acquisition is known to alter coronal alignment measurements on LLRs.[23]

The EOS 2D/3D system[30,31] is a new technique that can be used to perform pre- and postoperative alignment measurements. Using 3D software, the system mathematically corrects for malpositioning during acquisition, thus measurements are more valid.[32,33] Because the system scans the lower limb using a C-arm, there is no divergence in the vertical plane. Performing coronal alignment measurements both pre- and postoperatively with EOS 3D has been proven to be valid and reliable.[34,35] With the EOS 3D system, these measurement errors due to malpositioning are eliminated.[32,33] Also, validity of the images may be improved since divergence in the vertical plane is diminished.

Aim of this study was therefore to compare CAS alignment measurements during the primary TKA procedure with pre- and postoperative coronal alignment measurements using EOS 3D reconstructions.

MATERIALS AND METHODS

Design

We prospectively collected data of patients who underwent primary TKA with

CAS (CAS-TKA) using the ORTHOsoft Navitrack system (Zimmer inc., Warsaw, IN, USA) between December 2012 and November 2014. The surgeries were performed by two orthopaedic surgeons (SKB and ALB) who have extensive experience with the use of CAS during TKA. Informed consent was obtained from all individual participants included in the study. In accordance with regulations of the Medical Ethical Review Board of the University Medical Center Groningen, patients were informed about the fact that data of their CAS measurements and radiographs could be used for scientific research. If patients had objections to the use of their data, these data were not included in the study.

Procedure

Alignment measurements investigated in this study were:

- Varus/valgus angle of the leg (VV): the angle between the line from the femoral head to the centre of the knee and the line from the centre of the ankle to the centre of the knee in the coronal plane.

- Mechanical lateral distal femoral angle (mLDFA): the angle between the mechanical axis of the femur and the tangent to the distal parts of the condyles in the coronal plane.

- Mechanical medial proximal tibial angle (mMPTA): the angle between the mechanical axis of the tibia and the tangent to the tibial plateau in the coronal plane.

Intraoperative CAS measurements were performed and saved twice: the VV, mLDFA and mMPTA were measured before any surgical interventions were performed, and the VV was measured again after implantation of the knee prosthesis. The VV was measured with the leg in extension and the patella reduced while performing slight axial pressure, mimicking a weight bearing measurement. The first CAS measurements were compared with the preoperative EOS 3D measurements and the second CAS measurement was compared with the postoperative EOS 3D measurement.

Anteroposterior (AP) and lateral (LAT) X-rays were made of all patients

pre- and postoperatively using the EOS 2D/3D system (EOS Imaging, Paris, France) as part of the standard TKA protocol. Patients were positioned on the EOS platform in standing position with one foot 10 cm in front of the other. Next, an orthogonal AP and LAT image of the leg was taken, scanning the leg from the foot up to the hip in order to create weight bearing images. The images were anonymised by removing names and patient numbers. SterEOS software (EOS Imaging, Paris, France) was used to create 3D reconstructions of these AP and LAT images. The 3D reconstructions were performed by one of the authors (MFM), who had done >100 EOS 3D reconstructions before the start of this study. Of the preoperative images, 3D reconstructions were performed following the guidelines of the manufacturer.[36] For all angles, a negative (-) value indicated varus and a positive (+) value indicated valgus. Since several landmarks disappear or change when a knee prosthesis is implanted, the adjusted guidelines as we have described earlier [35] were followed for postoperative 3D measurements. Since the distal femur and proximal tibia were replaced by prosthetic components, only the VV could be measured in 3D on the postoperative images.

Statistical analyses

For statistical analysis, IBM SPSS Statistics for Windows software (Version 22.0, Armonk, NY: IBM Corp.) was used. Potential differences in means between the CAS and EOS measurements were compared using a paired Student T-test. Correlations between the CAS and EOS measurements were determined using Spearman's Rho and were interpreted according to the benchmarks described by Domholdt[37]: a 0.90-1.00 represents a very strong correlation, 0.70-0.89 a strong correlation, 0.50-0.69 moderate, 0.26-0.49 weak and 0.00-0.25 represents little if any correlation.[37] The Bland & Altman method was used to examine heteroscedasticity and potential biases between the CAS and EOS measurements.[38] When zero lies within the 95% CI, no bias exists between the measurements.[39] For the Bland & Altman method the mean VV angles of the CAS and the EOS measurements were calculated. The mean differences between the CAS and EOS measurements

were also calculated by subtracting the angle measured by the EOS system from the angle measured by CAS. Cohen's coefficients were calculated to investigate agreement in the number of outliers as measured with CAS and EOS.[40] A deviation of >3˚ varus or valgus from the neutral axis was considered an outlier.[1] The values were interpreted according to Landis and Koch [41]: <0 represents less than chance agreement, 0.01-0.20 represents slight agreement, 0.21-0.40 fair agreement, 0.41-0.60 moderate agreement, 0.61-0.80 substantial agreement and 0.81-0.99 almost perfect agreement. chi-square tests were performed to assess statistically significant differences in the number of outliers. For all statistical analyses, a p-value of <0.05 was considered to indicate statistical significance.

RESULTS

In this study, 52 primary TKA patients (56 knees) were included. The group consisted of 18 males and 34 females with a mean age of 60 ± 9.6 years (range 36–82). Fifty knees were available to compare CAS measurements to the preoperative EOS measurements, and 50 knees to compare CAS to postoperative EOS measurements. Due to errors of the navigation system or when a navigation tracker had to be removed because it blocked surgical instruments, only the first CAS measurement was used in some cases. Also, one patient had a fracture at the location of the tibial tracker, therefore it was decided to exclude the postoperative EOS measurement.

When the CAS measurements were compared with the preoperative EOS measurements there was a significant difference between the VV angle measured using CAS (VVCAS) and the VV angle measured using EOS (VV3D), the mean VVCAS being 3.04˚ (95% CI: 1.5˚–4.6˚ (P ≤ 0.001)) more valgus than the VV3D (Table 1). The Bland & Altman plot showed heteroscedasticity (Fig. 1). This means that for varus legs the EOS measures a larger varus angle and for valgus legs it measures a larger valgus angle than CAS (Fig. 2). Correlation between the two measurement techniques was strong and the coefficient showed fair agreement of the number of outliers (Table 1).

There was no significant difference between the mLDFA measured

using CAS and EOS (P = 0.12) (Table 1) and no systematic bias (Fig. 3). Correlation between the CAS and EOS measurements was strong and there was moderate agreement on the number of outliers (Table 1). A significant difference was found between the measurement of the mMPTA using CAS and EOS (P = 0.01) (Table 1). The mean difference was 1.86˚ (95% CI: 0.47˚–3.25˚) with the CAS measuring more valgus; this was confirmed with a systematic bias using the Bland & Altman method (Fig. 4). Correlation between the two measurement techniques was moderate and the coefficient showed a moderate agreement on the number of outliers (Table 1).

When the second VVCAS measurement was compared to the postoperative VV3D measurement, a significant difference was found (mean difference: 2.23˚ (95% CI: 1.2˚–3.3˚) (P ≤ 0.001) (Table 1). The Bland & Altman plot showed that the CAS systematically measured more valgus than the EOS (Fig. 5). Correlation between the CAS and EOS measurements was moderate and the coefficient showed slight agreement on the number of outliers (Table 1).

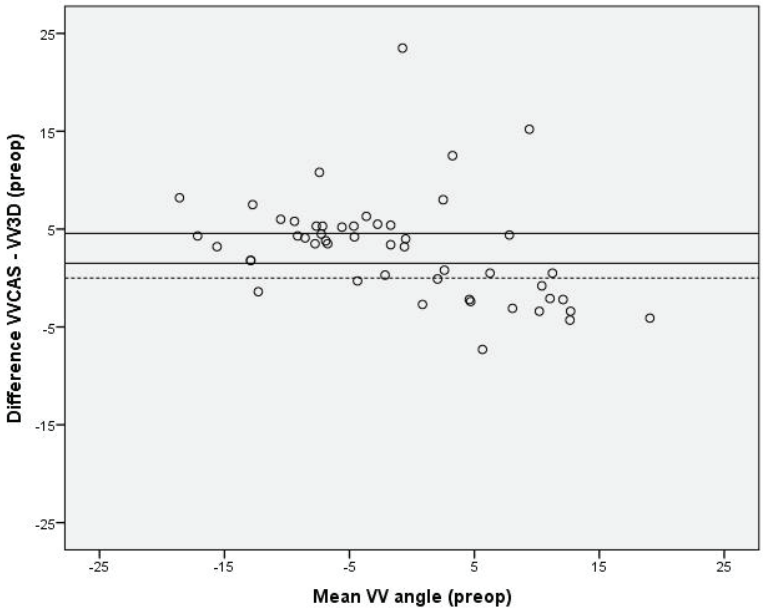

Figure 1. Bland & Altman plot of the primary CAS measurement and preoperative EOS measurement of the varus/valgus angle, showing heteroscedasticity

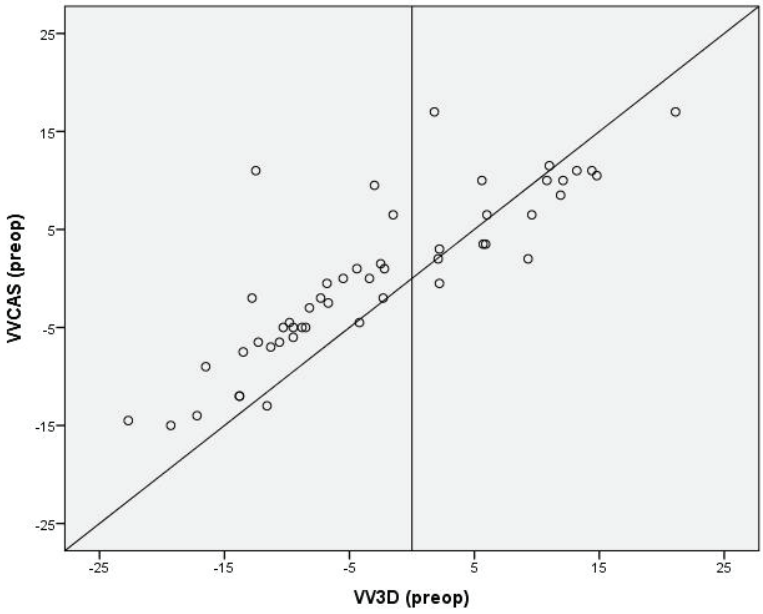

Figure 2. For varus legs EOS measures more varus and for valgus legs it measures more valgus compared than CAS

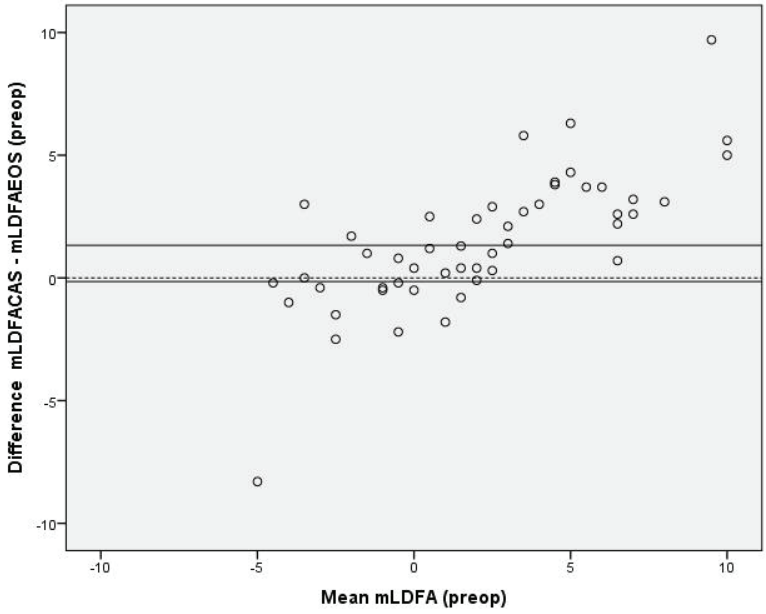

Figure 3. Bland & Altman plot of the primary CAS measurement and preoperative EOS measurement of the mechanical lateral distal-femoral angle, showing no systematic bias

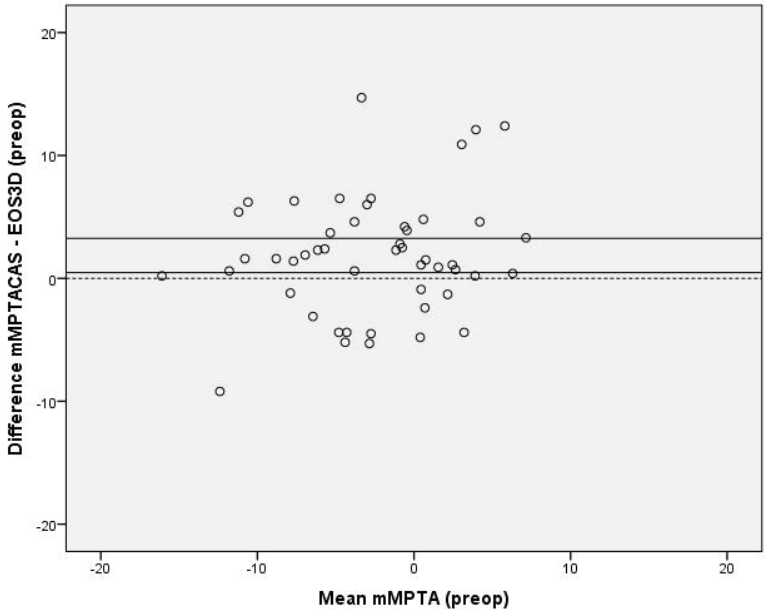

Figure 4. Bland & Altman plot of the primary CAS measurement and preoperative EOS measurement of the mechanical medial proximal tibial angle, showing a systematic bias

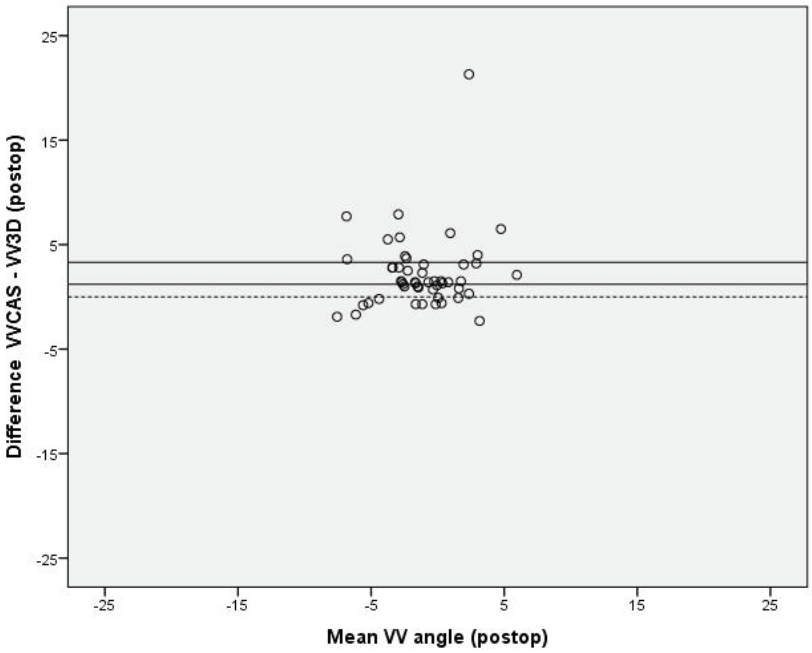

Figure 5. Bland & Altman plot of the second CAS measurement and postoperative EOS measurement of the varus/valgus angle showing a systematic bias

Table 1: Comparison of CAS and EOS measurements

Before implantation of prosthesis								
	Mean	SD	Mean difference (95% CI)	SDΔ	Range of difference CAS-EOS	P-value	Spearman's rho	Kappa
VVCAS	0.19	8.3						
VV3D	-2.85	10.3	3.04 (1.5 – 4.6)	5.4	-7.3 – 23.5	≤0.001*	0.87	0.34
mLDFA CAS	2.08	3.9						
mLDFA EOS	1.49	2.8	0.59 (-0.2 – 1.3)	2.6	-6.5 – 5.8	0.12	0.76	0.58
mMPTA CAS	-1.73	6.3						
mMPTA EOS	-3.59	5.5	1.86 (0.4 – 3.3)	4.8	-9.2 – 14.7	0.01*	0.67	0.44
After implantation of prosthesis								

SD = standard deviation; 95% CI = 95% confidence interval; CAS = computer-assisted surgery; VVCAS = varus/valgus angle measured using CAS; VV3D = varus/valgus angle measured in 3D using EOS; mLDFA = mechanical lateral distal-femoral angle; mMPTA = mechanical medial proximal tibial angle. To calculate the mean difference, the angle measured by the EOS system was subtracted from the CAS angle. A * indicates statistical significance (P <0.05)

DISCUSSION

The most important finding of the present study was that the intraoperative CAS measurements during TKA differed from almost all EOS 3D pre- and postoperative coronal alignment measurements. VV measurements using CAS measured a smaller angle for both varus and valgus legs when compared to the preoperative EOS measurements. CAS showed a significantly larger valgus angle than the preoperative EOS 3D measurement of the mMPTA. The preoperative measurement of the mLDFA did not show any significant difference. VV measurements of CAS compared to the postoperative EOS measurements had significantly more valgus.

Previous studies have shown discrepancies between intraoperative CAS measurements and pre- and postoperative alignment measurements.[25-29] Several factors have been mentioned as a possible explanation for this difference: the influence of malpositioning during acquisition of LLRs on alignment measurements, the validity and reliability of alignment measurements on LLRs, the influence of a weight bearing position on alignment measurements, and errors in the validity and reliability of CAS measurements. Radiological alignment measurements on standard LLRs are prone to measurement errors because of malpositioning during acquisition. Lower limb deformities, rotation and flexion contracture alone or in combination influence the validity of alignment measurements on LLRs.[21-24] In previous studies comparing CAS measurements with radiographic measurements this has been one of the main explanations for the differences found. In our study, however, we used EOS 3D reconstructions to measure alignment on LLRs. When performing a 3D reconstruction, the potential bias caused by leg deformity or malpositioning is eliminated,[32] therefore this factor is not likely to exert a major influence on the measurements taken. This phenomenon is also shown in an experiment conducted by our research group,[33] where an artificial leg containing a knee prosthesis was placed in several different positions. LLRs were made and 2D measurements and 3D reconstructions were performed for these different positions. We concluded that 2D alignment measurements differed considerably from the preset angle of the artificial leg, while the 3D reconstructions showed small deviation.[33]

Besides validity, we have also showed excellent intra- and interobserver reliability when performing knee prosthesis alignment measurements using EOS 3D reconstructions.[35]

The difference between the supine and weight bearing position of the patient may be an important reason for measurement differences. Coronal alignment of the knee is a dynamic parameter that can be influenced by both a weight bearing position and the amount of flexion in the knee. Three studies[42-44] have compared alignment measurements in supine and weight bearing position, finding significant differences between both measurement methods. Brouwer et al.[42] and Specogna et al.[43] found an average of respectively 2˚ and 1.5˚ more varus in the weight bearing position than in the supine position. However, these studies only included knees with a varus deformity. Sabharwal et al.[44] found that patients with a substantial mechanical axis deviation were more likely to show differences in outcome of measurements in supine and weight bearing position. This may also be the reason why the EOS measurements showed a larger varus angle for varus legs and a larger valgus angle for valgus legs compared to the supine CAS measurements. Overestimation of the VV angle on LLRs was also reported in three other studies comparing CAS and radiographic measurements.[26,28,29] We did not find this effect for the postoperative EOS measurements. Our hypothesis is that after implantation of the prosthesis substantial mechanical axis deviations and ligamentous imbalances were corrected. The effect of a weight bearing position is most distinct for larger VV angles and laxity of collaterals.

The validity and reliability of CAS measurements may play an important role in the measurement differences. Hauschild et al.[17] reported that alignment measurements using CAS are highly valid, but these measurements are prone to error when the knee is flexed. A cadaveric study investigating intraobserver errors when obtaining visually selected anatomical landmarks showed a maximum error of the VV of 1.32˚, but this was done on bone stripped of all soft tissue, making it easier to register the landmarks.[19] A second study conducted by the same research group showed an error of 0.7˚ for the VV. In addition, low reliability of the registration of

anatomical landmarks and significant interobserver differences were found.[20] A study comparing CAS, LLR and CT measurements found that LLR and CT correlated well, but CAS did not correlate well with LLR or CT. This raises the question about the reliability of intraoperative CAS measurements.[25] Intraoperative changes, such as movement of the trackers, may also be of influence on the CAS measurements. Although these studies report on the results of imageless CAS systems, none investigated the specific CAS system we used. Reliability and validity may also be dependent on the design and software of a specific system, hence it can be questioned whether results of studies regarding other systems are applicable to the system used in our study.

It is suggested that correlation between CAS and radiographic measurements after TKA may be influenced by the moment of acquisition of the postoperative radiographs. Hauschild et al.[27] compared two groups who underwent CAS-TKA. One group received LLRs two weeks postoperatively and the other group three months postoperatively. Correlations between radiographic measurements using CAS and LLRs taken three months postoperatively were excellent, but were poor when the intraoperative CAS measurements were compared with alignment measurements performed on LLRs taken two weeks postoperatively. They hypothesised that after three months patients are usually able to bear full weight and full or near-full extension of the knee, which improves correlation between alignment measurements using CAS and postoperative LLRs. The moment of assessment of the postoperative LLRs may thus be of influence. However, the fact that an LLR is made when applying full weight bearing would theoretically cause a larger difference between CAS and LLR measurements instead of a smaller difference, as CAS measurements are non-weight bearing. Also, the conclusions of the study performed by Hauschild et al.[27] were drawn from a comparison of two patient samples. It might be that the differences found between the two acquisition moments are not based on time but on patient factors. In our study postoperative LLRs were taken at six weeks postoperatively, at which point patients are generally able to apply full weight on their operated leg and can extend the knee. Moreover, the EOS

system corrects malpositioning during acquisition, including flexion of the knee,[33] therefore the moment of acquisition is not expected to influence the results found in our study.

This study has some limitations. First of all, the LLR measurements were performed by a single observer. It should however be noted that this observer has extensive experience performing EOS 3D reconstructions, and interobserver reliability of EOS 3D measurements has proven to be excellent.[35] Secondly, a potential bias might be present during the CAS measurements. When performing preoperative planning, leg alignment measurements are taken and the first intraoperative CAS measurements cannot be blinded, as that is not possible in this setup. The orthopaedic surgeon might therefore be potentially biased when performing the first CAS measurement. Although the second CAS measurement was not blinded either, measurement bias is unlikely as the outcome of postoperative EOS measurements during TKA is not known.

CONCLUSION

The results of this study indicate that differences in alignment measurements between CAS and pre- and postoperative LLRs are mainly due to the difference between weight bearing and non-weight bearing positions, as well as potential errors in validity and reliability of the CAS system. Surgeons should be aware of these measurement differences and the pitfalls of both measurement techniques. Further research is required to gain more insight into the validity and reliability of navigation systems.

CONFLICT OF INTEREST

One of the authors (ALB) will be and has been paid as a consultant for Zimmer (Warsaw, IN, USA) for purposes of education and training in knee arthroplasty. The department receives research institutional support from InSpine (Schiedam, The Netherlands) and Stryker (Kalamazoo, MI, USA) but this support is not of influence of this study. The other authors declare that they have no conflict of interest.

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Chapter 7

The influence of computer-assisted surgery on rotational, coronal and sagittal alignment in revision total knee arthroplasty

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ABSTRACT

Background: Despite good results of primary total knee arthroplasty (TKA), the number of revision total knee arthroplasties (rTKAs) is rising. Proper implant position is essential, since malposition leads to worse clinical outcome. In rTKA most anatomical landmarks have disappeared because of extensive bone loss, making it more difficult to adequately implant the knee prosthesis. In primary TKA, computer-assisted surgery (CAS) leads to better prosthetic alignment than mechanical navigation guides. Literature about the use of CAS in rTKA is scarce though, and the effect on rotational prosthetic alignment has not been investigated yet. Hence the primary objective of this study is to compare rotational prosthetic alignment when using CAS in rTKA compared to a mechanical navigation guide. Secondary objectives are to compare prosthetic alignment in the coronal and sagittal planes. It is hypothesized that CAS leads to better rotational, coronal and sagittal prosthetic alignment when used during rTKA.

Methods/design: A prospective clinical intervention study with use of a historical control group will be conducted. Forty-four patients with a minimum age of 18 to be admitted for CAS-rTKA between September 2012 and September 2015 will be included in the intervention group. Forty-four patients with a minimum age of 18 who underwent rTKA with the use of a mechanical navigation guide between January 2002 and April 2012 will form the historical control group. Both groups will be matched according to gender and type of revision prosthesis. Rotational prosthesis alignment will be evaluated using a CT-scan of the knee joint.

Discussion: Proper implant position is essential, since malposition leads to worse clinical outcome. Several studies show a significantly positive influence of CAS on prosthetic alignment in primary TKA, but literature about the use of CAS in rTKA is limited. The purpose of this study is thus to investigate the influence of CAS during rTKA on postoperative prosthetic alignment, compared to mechanical navigation guides.

Trial registration: Netherlands National Trial Register NTR3512

BACKGROUND

Osteoarthritis (OA) is one of the most prevalent age-related musculoskeletal conditions. Although OA may affect any joint of the body, it is most commonly seen in the hip and knee.[1] OA of the knee leads to a significant impairment in patients' ability to perform activities of daily living and has a large impact on health-related quality of life.[2,3] For advanced OA of the knee, total knee arthroplasty (TKA) is a highly successful and widely applied surgical treatment, with 450,000 primary TKAs performed in the United States in 2005[4] and 21,475 TKAs in the Netherlands in 2010.[5] Due to a growing elderly population and changing thresholds for surgery, these numbers are expected to increase dramatically in the coming decades.[4,6]

As a result, the number of TKA revisions (rTKA) will also increase. The demand for rTKA is expected to double by 2015 and a growth of 601% is predicted for the United States between 2005 and 2030.[7] A similar trend is expected for other Western countries. Main reason for rTKA is aseptic loosening, which accounts for 30-42% of all rTKAs. Infection is the second most common indication and is responsible for about 20% of all revisions. Other reasons for rTKA may be pain, instability, wear, fracture, malalignment, implant breakage, incorrect size and dislocation of one or more components.[8,9] Main reasons for rerevision after rTKA are infection (35-46%), followed by aseptic loosening (19-30%). Other reasons for rerevision are wear/osteolysis, instability, stiffness and periprosthetic fractures.[10,11]

The goal of both primary and revision TKA is to restore function and stability of the knee joint and to alleviate pain. However, rTKA is a more complicated surgical procedure than primary TKA and leads to worse clinical results. Major differences between revision and primary TKA are the amount of bone loss and ligamental damage.[12,13] Reasons for this are osteolytic lesions caused by wear, aseptic loosening or infection, and removal of the primary implant.

Proper positioning of the implant is important, since malpositioning of a knee prosthesis leads to worse patient outcome and wear of the prosthesis.[14] Optimal prosthetic alignment is therefore an essential part of the

surgical procedure. In primary TKA, one can identify anatomical landmarks and use them to determine the position of the implant using mechanical navigation guides. However, in rTKA most of the time anatomical landmarks have disappeared because of extensive bone loss, making it more difficult to adequately implant the prosthesis.

Several computer navigation systems have been developed to improve prosthetic alignment. In primary TKA, computer-assisted surgery (CAS) is shown to lead to better prosthetic alignment than mechanical alignment guides.[15-23] Several studies have shown improved postoperative mechanical axis as well as coronal, sagittal and rotational prosthetic alignment when using CAS during primary TKA.[15,16,24] Perlick et al.[25] revealed a significantly better mechanical limb axis and coronal alignment of the femoral component when CAS was used during rTKA. However, literature about the use of CAS in rTKA is scarce[25,26] and potential differences in rotational alignment of the prosthesis have not yet been investigated. It is hypothesized that CAS also results in a more accurate prosthetic alignment when used in rTKA. Correct alignment of the prosthesis is more difficult during rTKA compared to primary TKA because of extensive bone loss and the disappearance of anatomical landmarks. This may imply that one can expect more advantages from CAS in rTKA than from primary TKA.

Hence the primary objective of this study was to investigate the effect of CAS on rotational prosthetic alignment when used in rTKA. The effect of CAS on prosthetic alignment in the coronal and sagittal planes will also be determined.

METHODS/DESIGN

Study design

A prospective clinical intervention study with use of a historical control group will be conducted. In the prospective intervention group patients will undergo rTKA using CAS. These surgeries will take place between September 2012 and September 2015. The historical control group will consist of patients who

underwent rTKA between January 2002 and April 2012. The intervention and control groups will be matched according to gender and type of revision prosthesis. The study design, procedures and informed consent are approved by the Medical Ethics Committee of University Medical Center Groningen (UMCG).

Study population

The study will be conducted at the Orthopedic Department of UMCG. Inclusion criteria for the intervention group are:

- Use of CAS during rTKA.

- Minimum age of 18 years.

- Total revisions, re-implantations and partial revisions of either the tibial or the femoral part are included. For partial revisions, only measurements of the part of the prosthesis to be revised will be used.

Inclusion criteria for the historical control group are:

- rTKA without the use of CAS.

- Minimum age of 18 years.

- Total revisions, re-implantations and partial revisions of either the tibial or the femoral part are included. For partial revisions, only measurements of the part of the prosthesis that was revised will be used.

- Patients will be included if the NexGen® revision system (Zimmer Inc., Warsaw, Indiana, USA) was used.

Exclusion criteria for both groups are:

- Insert replacements and placement of a patellar button only.

- Patients who receive a tumor prosthesis during rTKA.

- Patients with a limited knowledge of the Dutch language or who are mentally incapable of participating.

In both the intervention group and the historical control group the anesthetic, analgesic and postoperative physiotherapy protocols are identical.

Surgical procedure rTKA

rTKA can be described in three steps: 1) removal of implant, 2) classification of defects and 3) rebuilding of joint by "tibia first technique". The first step is to extract the failing components and to remove all debris to create a new situation. Hereby bone will be preserved as much as possible, although bone of poor quality has to be removed.

The second step is to classify the bone defects according to the Anderson Orthopaedic Research Institute (AORI).[27] In defect types 2a, 2b and 3 bone loss will be compensated by metal augmentations, while stems attached to the tibial and femoral components will spread the load to the implant interfaces to secure fixation.

The third step is the rebuilding of the knee joint with a revision prosthesis. The NexGen® revision system (Zimmer Inc., Warsaw, Indiana, USA), is used at the Department of Orthopedics of UMCG. Depending on the bone defects the NexGen Legacy Condylar Constraint Knee® (LCCK) (type 2a or 2b) or the NexGen Rotating Hinge Knee® (RHK) (type 3) is used. Tibial and femoral revision components are placed with press-fit stems, and if needed with augmentation blocks or trabecular metal cones. The revision prosthesis is fixed with bone cement (Refobacin® revision bone cement with clindamycin and gentamicin, Biomet Inc., Warsaw, Indiana, USA). Depending on the stability and integrity of the collateral ligaments, the type of articulating surface is chosen during surgery. With good collateral ligaments a posterior stabilizing component (Legacy Posterior Stabilized®, LPS) will give sufficient stability. However, in case of coronal plane instability a semi-constraint insert (LCCK) with a high post is needed. With gross collateral deficiency and

multidirectional instability a rotational hinge is the best choice (RHK).

Intervention group

In the intervention group, CAS will be applied during rTKA. The ORTHOsoft Navitrack® navigation system (Zimmer Inc., Warsaw, Indiana, USA) will be used. The navigation is based on an infrared reflecting system with use of trackers in the femur and tibia. The system guides the surgery by an image-free model based on anatomical landmarks identified by the surgeon. After the exposure a femoral tracker is placed proximally from the knee in the same knee wound or in an additional 3-cm incision. The tibial tracker will be placed in an additional 3-cm incision above the ankle. Before removal of the primary prosthesis, the navigation protocol is applied in which the anatomical landmarks are chosen and the system will build its model from the patient's data. Thus, all anatomical landmarks are identified with the primary prosthesis in situ. The mechanical axis of the lower limb as measured with this system is the angle between the mechanical axis of the femur and tibia. The mechanical axis of the femur is the axis between the center of the femoral head and the deepest point of the intercondylar notch. The center of the femoral head is determined by moving the leg in a conical pattern, digitizing 14 distinct positions of the femoral tracker. The deepest point of the intercondylar notch is marked by the orthopedic surgeon. The mechanical axis of the tibia is the axis between the entry point of the proximal medullary canal and the center of the ankle. The entry point of the medullary canal is marked by the orthopaedic surgeon and the center of the ankle is assessed by marking the medial and lateral malleoli. Coronal and sagittal prosthesis alignment of the femoral and tibial components are calculated according to respectively the femoral and tibial mechanical axis. Rotation of the femoral component is determined according to the epicondylar axis. The orthopaedic surgeon marks the medial and lateral epicondyle and thus this axis is generated. Rotation of the tibial component is assessed in relation to the axis between the middle of the posterior cruciate ligament insertion and the medial third of the tibial tuberosity. Both landmarks are marked by the orthopaedic surgeon. The navigation system will guide the surgery in positioning the components and choosing the size of the implants.

When implanting a press-fit stem, it may be that alignment of the components are influenced by the stem. After removal of the primary prosthesis and preparation of the bone cuts, different provisional components are tried in order to determine the correct type and size of the components. In this way, and by checking the alignment of the components with the navigation system, the orthopaedic surgeon will know if the stem influences the component alignment. In the revision system we have the availability of straight stems and off-set stems to use the best position of the component in combination with the stem but not forced by the stem. When this is the case, a stem of a smaller diameter will be chosen, so that the components are placed according to the bone cut made using the navigation system instead of the stem. Cementing underneath the tibial tray and leaving the stem uncemented generally provides enough component stability. In the rare case of the components not being rotationally stable, the stem will be cemented.

Historical control group

In the control group the position of the revision prosthesis was determined using mechanical intramedullary alignment guides for the femur and tibia. Positioning of the components and sizing were based on the same anatomical landmarks as in the intervention group with use of prototypes and trial components.

Study procedures

Demographic characteristics, BMI, indication for operation, type and brand of prosthesis, total amount of blood loss, surgical time, length of hospital stay and ASA classification will be collected and/or recorded for all patients included in this study.

Radiographic evaluation

Rotational prosthetic alignment will be measured on a CT-scan of the operated leg. For evaluation of alignment in the coronal and sagittal planes a new imaging device, called the EOS system (Biospace Imaging, Paris, France),[28] will be used. This device is characterized by a reduction in radiation (800-1000 times less than for CT-scan and 10 times less than conventional X-ray).[28,29] Reason for this is the use of an innovative technology called fast gaseous particle detectors, invented by George Charpak (which earned him the Nobel prize in physics in 1992). The EOS imaging device uses two orthogonal sources of radiation and linear detectors that are coupled together. These sources move up and down along the patient, producing an anterior-posterior and lateral image at the same time while the patient is in weight bearing position. This is a different technique than conventional radiograph systems, where beams are divergent in horizontal and vertical plane.

Of the patients in the intervention group, a CT-scan of the operated leg will be made postoperatively during the visits at the outpatient clinic. Patients included in the historical control group have already undergone the standard surgical technique for rTKA. A CT-scan of the operated leg will be made the next time the patient visits the outpatient clinic of the Orthopedic Department for follow-up of the rTKA.

For evaluation of rotational prosthetic alignment, rotation of the femoral and tibial components will be determined separately according to the Berger CT protocol.[30] Angles measured for rotational alignment are:

- Condylar twist angle for rotation of the femoral component: angle between the epicondylar axis and the prosthetic posterior condylar axis (inner border of posterior cut). Endorotation of the femoral component will be shown as a positive (+) angle and exorotation of the femoral component will be shown as a negative (-) angle. An angle of >3° endorotation or exorotation will be considered an outlier.

- Rotation of the tibial component: angle between the tibial tubercle axis (axis between the geometric center of the proximal tibial plateau and the tip of the tubercle) and the tibial component angle (anterior-

posterior line through the tibial component). Normal rotation of the tibial component is considered 18˚ endorotation.[30] Endorotation of the tibial component will be shown as a positive (+) angle and exorotation of the tibial component will be shown as a negative (-) angle. An angle of >3˚ endorotation or exorotation will be considered an outlier.

Prosthetic alignment in the coronal and sagittal planes will be measured using postoperative coronal and sagittal X-rays of the operated leg. These lower-limb X-rays are obtained using the EOS system (Biospace Imaging, Paris, France)[28] EOS 2D images will be used for measuring alignment. For the intervention group, standard coronal and sagittal X-rays will be taken postoperatively as part of the standard operation protocol. For the historical control group, standard coronal and sagittal X-rays have already been taken postoperatively.

Angles measured for coronal and sagittal alignment are:

- Mechanical angle of the leg (HKA): Angle between the line from the femoral head to the center of the knee and the line from the center of the ankle to the center of the knee in coronal plane.

- Mechanical lateral distal-femoral angle (mLDFA): Angle between the mechanical axis of the femur and the articular surface of the femoral part of the prosthesis in coronal plane.

- Mechanical medial proximal tibial angle (mMPTA): Angle between the mechanical axis of the tibia and the articular surface of the tibial part of the prosthesis in coronal plane.

- Anatomical proximal posterior tibial angle (aPPTA): Angle between the mechanical axis of the tibia and the articular surface of the tibial part of the prosthesis in sagittal plane. Downslope of the design of Nexgen prostheses is 7°, and this angle is considered the normal aPPTA.

For the mechanical axis of the leg, mLDFA, mMPTA and aPPTA a generally accepted outlier cut-off of +/3° will be applied in this study.[31-34]

The canal-filling ratio (CFR) will be determined in both the intervention and control groups to assess whether the stems are canal-filling. The CFR will be measured on the coronal and sagittal EOS images as described by Parsley et al.[35] The stem diameter and endosteal diameter will be measured at the stem tip. The CFR will be calculated by dividing the stem diameter by the endosteal diameter. A stem is considered to be canal-filling when the CFR is ≥0.85.[35]

Sample size

The hypothesis is that the use of CAS leads to fewer outliers in prosthetic alignment compared to the use of mechanical alignment guides during rTKA. Primary outcome measure will be rotational prosthetic alignment. When using the conventional operation technique, around 25% of the knees is considered a radiological outlier. Therefore, a P2 value of 0.75 was chosen.[21,36] Previous research has shown that the use of CAS in TKA decreases the number of outliers by 17-30%.[21,37,38] When a 20% decrease in outliers is expected in the CAS group compared to the control group with P1=0.95, P2=0.75, power=80% and alpha=0.05, 44 patients per group are needed.

Since 2008 a total of amount of 21-30 rTKAs have been performed each year at UMCG, and an increase is expected. As a result of that, the possibility is expected of including 44 patients in the intervention group between September 2012 and September 2015. Inclusion of 44 patients in the historical control group is not expected to be a problem, as 165 rTKAs were performed between January 2002 and April 2012.

Statistical analysis

All statistical analyses will be performed using the PASW software package (version 19, SPSS, Chicago, USA). Descriptive statistics will be used to describe the main characteristics of both research groups. Differences in rotational,

coronal and sagittal alignment between the groups will be determined by using the nonparametric Mann-Whitney U-test for independent samples. For the clinical parameters, t-tests will be used for continuous values or the Mann-Whitney U-test when the variables are not normally distributed. A Chi-square test and a Fisher's Exact test will be used for dichotomous values. For all test procedures, a p-value of <.05 will be considered to indicate statistical significance.

DISCUSSION

Correct prosthetic alignment is important for a good clinical outcome after TKA. More accurate alignment after TKA correlates with less pain, better knee function, faster rehabilitation and improved quality of life.[39,40] Rotational malalignment has a negative effect on patellar tracking, stability, pain and overall biomechanics of the knee joint,[30,41-44] while malalignment in the coronal and sagittal planes leads to an increased risk of loosening, pain and instability.[31,34,45,46] Accurate prosthetic alignment is therefore essential during primary and revision TKA, to postpone revision and rerevision procedures.

In recent years, CAS has become a frequently used technique for improving prosthetic alignment in primary TKA, and several studies have shown its benefits. CAS significantly improves varus / valgus angle,[15,17-20,47] mLDFA,[16,17,21-23] mMPTA,[16,17,20,21,23] femoral flexion angle,[15,16,18,21,22] tibial downslope[15,18,20,22,23] and rotational alignment for the femoral and tibial components.[15,16,20] Perlick et al.[25] revealed a significantly better mechanical limb axis and coronal alignment of the femoral component when CAS was used during rTKA. Correct alignment of the prosthesis is even more difficult during rTKA compared to primary TKA because of extensive bone loss and the disappearance of anatomical landmarks. This may imply the expectation of an even greater advantage of CAS in rTKA compared to primary TKA. However, literature about the use of CAS in rTKA is scarce.[25,26,48,49] Moreover, patient groups in these studies are small and only one study has compared postoperative prosthetic alignment with a control group. Furthermore, potential differences in rotational alignment of the prosthesis have not yet

been investigated.

In conclusion, it is our expectation that this study will provide insight into the effectiveness of CAS in rTKA on postoperative prosthetic alignment. It is our hypothesis that the use of CAS in rTKA leads to improved prosthetic alignment compared to conventional rTKA.

COMPETING INTEREST

A.L. Boerboom is a paid consultant for Zimmer (Warsaw, IN USA) who does training in knee arthroplasty and computer-assisted surgery. The Department of Orthopedics of UMCG receives institutional research support from Zimmer (Warsaw, IN, USA). All other authors declare that they have no competing interests.

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Chapter 8

Does imageless computer-assisted TKA lead to improved rotational alignment or fewer outliers? A systematic review

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ABSTRACT

Background: Computer-assisted surgery (CAS) has been developed to enhance prosthetic alignment during primary TKAs. Imageless CAS improves coronal and sagittal alignment compared with conventional TKA. However, the effect of imageless CAS on rotational alignment remains unclear.

Questions/purposes: We conducted a systematic and qualitative review of the current literature regarding the effectiveness of imageless CAS during TKA on (1) rotational alignment of the femoral and tibial components and tibiofemoral mismatch in terms of deviation from neutral rotation, and (2) the number of femoral and tibial rotational outliers.

Methods: Data sources included PubMed, MEDLINE, and EMBASE. Study selection, data extraction, and methodologic quality assessment were conducted independently by two reviewers. Standardized mean difference with 95% CI was calculated for continuous variables (rotational alignment of the femoral or tibial component and tibiofemoral mismatch). To compare the number of outliers for femoral and tibial component rotation, the odds ratio and 95% CI were calculated. The literature search produced 657 potentially relevant studies, 17 of which met the inclusion criteria. One study was considered as having high methodologic quality, 15 studies had medium, and one study had low quality.

Results: Conflicting evidence was found for all outcome measures except for tibiofemoral mismatch. Moderate evidence was found that imageless CAS had no influence on postoperative tibiofemoral mismatch. The measurement protocol for measuring tibial rotation varied among the studies and in only one of the studies was the sample size calculation based on one of the outcome measures used in this systematic review.

Conclusions: More studies of high methodologic quality and with a sample size calculation based on the outcome measures will be helpful to assess whether imageless CAS TKA improves femoral and tibial rotational alignment and tibiofemoral mismatch or decreases the number of femoral and tibial rotational outliers. To statistically analyze the results of different studies, the same measurement protocol should be used among the studies.

INTRODUCTION

The main reason for revision TKA is aseptic loosening, which in two studies caused 30% and 42% of all revisions, respectively.[1,2] Malpositioning of a knee prosthesis leads to worse functional outcome and increased wear, which eventually may lead to revision,[3,4] and malalignment in some planes has been shown to result in an increased risk of aseptic loosening. Specifically, malalignment in the coronal and sagittal planes results in an increased risk of aseptic loosening, pain, and instability,[5-8] and rotational malalignment has a negative effect on patellar tracking, stability, pain, and joint biomechanics.[9-13] Good alignment correlates with better functional outcome, as measured by The Knee Society Score© and Short Form-12, and faster rehabilitation after TKA.[14,15] Owing to the importance of correct alignment, computer-assisted surgery (CAS) was developed. There are two different techniques in CAS: image-based and imageless computer navigation. When using image-based navigation, preoperative CT, MRI, or intraoperative fluoroscopy is used for the software to generate a lower-limb model. With imageless CAS, the lower-limb model is made based on anatomic landmarks that are marked preoperatively. With a CAS TKA, imageless navigation is used mostly in daily practice. The use of imageless CAS has been shown to improve coronal and sagittal alignment compared with conventional TKA.[16-21] Whether the use of imageless CAS also improves clinical or functional outcome or survivorship is unknown, since studies regarding this are scarce and have a short followup.[22-24]

However, the influence of imageless CAS on rotational alignment is unclear. To date, three reviews have taken the influence of rotational component orientation into account.[25-27] Burnett and Barrack[25] performed a narrative review and found limited evidence of improvement of rotational alignment. They concluded that strong statistical heterogeneity existed among the studies. A systematic review by Cheng et al.[26] showed no decrease in the number of rotational alignment outliers of the femoral or tibial component after imageless CAS TKA. In another systematic review, Hetaimish et al.[27] also found no decrease in the number of femoral rotational outliers after imageless CAS TKA. However, these conclusions should be interpreted with

caution. First, the number of included studies in both systematic reviews was low: only six[26] and four[27] studies were included. Second, only randomized controlled trials (RCTs), quasi-RCTs, and prospective comparative studies were included. Including studies other than RCTs may provide important additional information.[28] Third, neither systematic review[26,27] took into account the methodologic quality of the studies. Finally, Hetaimish et al.[27] and Cheng et al.[26] covered published evidence until November 30, 2009, and August 30, 2010, respectively. Since August 30, 2010, six studies comparing alignment after imageless CAS TKA versus conventional TKA have been published.[18,19,29-32]

The aim of our study was to conduct a systematic and qualitative review of the current literature on the effectiveness of imageless CAS during TKA on (1) rotational alignment of the femoral and tibial components and tibiofemoral mismatch in terms of deviation from neutral rotation, and (2) the number of femoral and tibial rotational outliers.

SEARCH STRATEGY AND CRITERIA

This systematic review was conducted according to the guidelines presented in the PRISMA Statement.[33] An electronic literature search was conducted in PubMed, MEDLINE, and EMBASE for all studies published between 1991 and April 2, 2013. The search strategy consisted of the following components plus related MESH and free field terms for each: “knee arthroplasty”, “computer assisted surgery”, “conventional”, and “rotation”. The search strategy was formulated and performed by an experienced medical librarian (TvI). To find more studies, the reference lists of all relevant studies were reviewed for potential articles.

We decided to include only imageless CAS and to exclude image-based CAS because imageless navigation systems are most commonly used in TKA. A study was included if (1) rotational alignment after imageless CAS TKA was compared with rotational alignment after conventional TKA; (2) the study design contained an intervention group and a control group, for example RCTs, cohort studies with a historical cohort as a control group, or

cadaveric studies with a control group; (3) the study subjects were 18 years or older; (4) the study and control groups were similar at baseline; (5) the study was published in English, Dutch, French, German, or Spanish; and, (6) at least one of the following outcome measures was assessed: rotational alignment of the femoral or tibial component, tibiofemoral mismatch, or number of rotational outliers of the femoral or tibial component. Rotation of the femoral component had to be measured relative to the epicondylar axis. Studies were excluded when rotational alignment was assessed using plain radiographs and when rotation of the femoral component was not determined according to the epicondylar axis.[34,35] A femoral rotational outlier was defined as greater than 3˚ deviation from the neutral position. As no gold standard exists for measuring tibial component rotation, we did not exclude studies regarding the tibial measurement protocol. A tibial rotational outlier was defined as greater than 3˚ deviation from the neutral position as determined in the measurement protocol used in the study. Tibiofemoral mismatch is the angle between the posterior condylar line of the femoral component and the AP line of the tibial component.

The procedure for inclusion of studies was performed in two stages according to the recommendations of van Tulder et al.[36]. Two reviewers (MFM, IHFR) independently selected the studies based on title, abstract, and full text. Disagreement was resolved by consensus, and if agreement was not achieved, a third reviewer was consulted (MS). The same two reviewers also extracted the data from the included studies independently. After conducting the electronic search and removing double citations, 657 potentially relevant studies remained (Fig. 1). After the selection procedure, 17 studies were included (Appendix).

The two reviewers independently assessed methodologic quality of the included studies according to criteria described by van Tulder et al.[36] Their 11 criteria relate to selection, performance, attrition, and detection bias. Adjustments had to be made to use their criteria for assessing methodologic quality in our systematic review. The requirement of blinding the patients or care providers was excluded because this is not possible in these types of studies. Blinding the orthopaedic surgeon is not possible because he or she

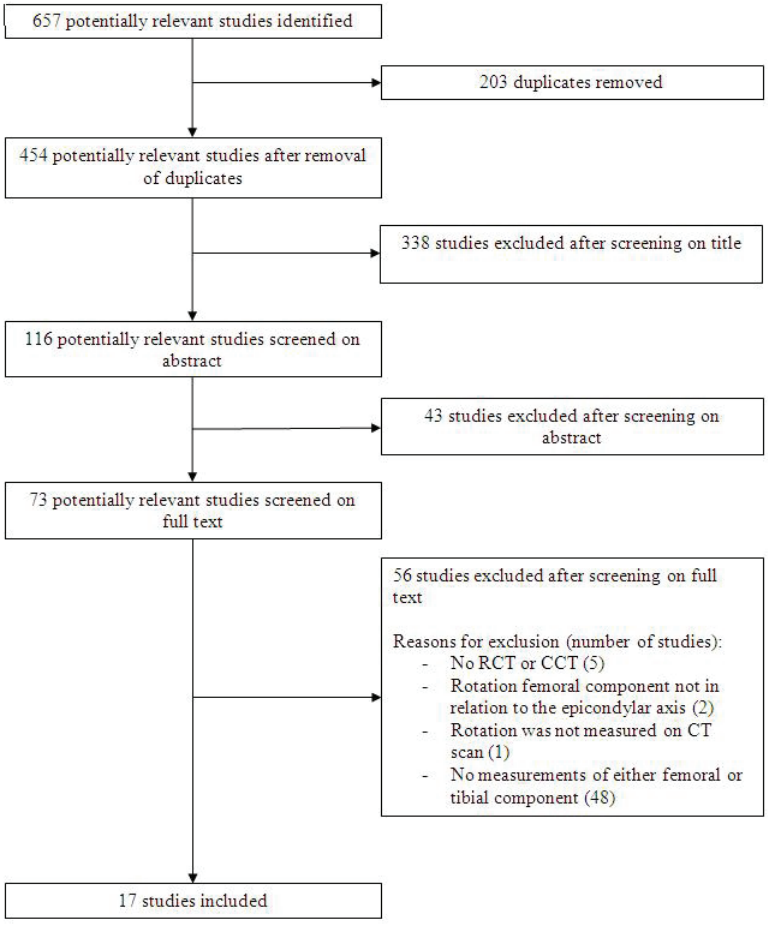

Figure 1. The flow chart shows the inclusion procedure. RCT=randomized controlled trial; CCT=controlled clinical trial.

performs the surgery. Blinding the patient is not possible because an extra incision at the distal tibia has to be made to place the navigation trackers when CAS is used during TKA. Patients who underwent conventional TKA do not have this extra incision. The requirement of acceptable compliance to the intervention also was excluded because this is not applicable in this type of intervention. Eight questions thus remained to be answered regarding methodologic quality of the studies. We added one more question: "Was a sample size calculation performed based on one of the three outcomes?" Insufficient power of a study has a low probability of detecting a statistically

significant difference. All criteria were answered with "yes," "no," or "unclear." A study was considered of high methodologic quality when at least six criteria were answered with "yes", a score of 3 to 5 was considered medium quality, and a score less than 3 was considered low quality. Methodologic quality of most studies was found to be medium. One study was considered high methodologic quality, 15 studies were medium quality, and one was low quality. The sample size calculation in only one of the included studies was based on one of the outcome measures used in this systematic review (Table 1).[37]

Analysis of the extracted data was conducted according to the guidelines for systematic reviews provided by the Cochrane Collaboration Group[36] using Review Manager 5 (Version 5.1; The Nordic Cochrane Centre, The Cochrane Collaboration, Copenhagen, Denmark). The standardized mean difference (SMD) with a 95% CI was calculated when possible for continuous variables (femoral and tibial component rotation and tibiofemoral mismatch). The SMDs were interpreted according to Cohen[46]: an SMD of 0.2 to 0.4 was considered a small effect, 0.5 to 0.7 moderate, and 0.8 or greater was considered a large effect. To compare the number of outliers for femoral and tibial component rotation, the odds ratio (OR) and 95% CI were calculated. Angles with a deviation greater than 3° internal or external rotation from the neutral rotational angle were considered outliers.[10] The OR represents the odds of outliers occurring in the CAS group compared with the conventional group with an OR less than 1 favoring the CAS group. The OR is considered statistically significant when the 95% CI does not include the value of 1.

Authors of articles were contacted to retrieve data of means and SDs to compute effect sizes or ORs where these data were not reported. Five authors sent additional data. The results were summarized by means of a qualitative analysis using a rating system that consists of five levels of scientific evidence taking into account the methodologic quality and outcome of the original studies (best evidence synthesis according to Van Tulder et al.[36]). Scientific evidence was considered strong when there were consistent findings among multiple high-quality trials. Evidence was considered moderate when consistent findings were found in multiple low-

quality trials and/or one high-quality trial. Evidence was considered limited when there were consistent findings in at least one low-quality trial. Evidence was considered conflicting when the findings among multiple trials (high and/or low quality trials) were inconsistent. There was no evidence when findings of the eligible trials did not meet the criteria for one of the levels of evidence as stated above, or when there were no eligible trials available. Consistent findings were defined as ≥75% of the trials showing results in the same direction.[36] We performed a sensitivity analysis to examine what the findings of the review would have been had we chosen different cutoff points to interpret the methodologic quality. For the sensitivity analysis, an internal validity score of 5 or greater was considered high quality, a score of 3 to 4 medium, and a score of 2 or less was considered low methodologic quality.

Table 1. Results of the methodologic quality assessment*

Study	Fulfilled validity criteria				Unfulfilled validity criteria	Incomplete information for validity assessment	Internal validity score	Methodologic quality	Power analysis
	Selection bias (1, 2, 3)	Performance bias (5)	Attrition bias (6, 8)	Detection bias (4, 7)					
Schmitt et al.[31]	1, 2, 3	-	8	4, 7	6	5	6	High	Unclear
Matos et al.[30]	1, 3	-	6, 8	7	-	2, 4, 5	5	Medium	Unclear
Chauhan et al.[38]	1, 2, 3	-	8	7	-	4, 5, 6	5	Medium	Unclear
Kim et al.[39]	1, 3	-	6, 8	4	-	2, 5, 7	5	Medium	Unclear
Lutzner et al.[37]	1, 3	-	6, 8	7	-	2, 4, 5	5	Medium	Yes
Mombert et al.[40]	1, 3	-	6, 8	7	-	2, 4, 5	5	Medium	Unclear
Blakeney et al.[18]	1, 3	-	-	4, 7	-	2, 5, 6, 8	4	Medium	No
Chauhan et al.[41]	3	-	6, 8	7	-	1, 2, 4, 5	4	Medium	Unclear
Han et al.[42]	1, 3	-	6, 8	-	-	2, 4, 5, 7	4	Medium	Unclear
Matziolis et al.[9]	1, 3	-	6, 8	-	-	2, 4, 5, 7	4	Medium	Unclear
Zhang et al.[19]	3	-	6, 8	4	-	1, 2, 5, 7	4	Medium	Unclear
Carter et al.[43]	3	-	6	4	1, 2, 7	5, 8	3	Medium	Unclear
Choong et al.[14]	1, 3	-	-	7	8	2, 4, 5, 6	3	Medium	No
Hiscox et al.[29]	-	-	6	4, 7	-	1, 2, 3, 5, 8	3	Medium	Unclear
Kim et al.[44]	3	-	8	4	-	1, 2, 5, 6, 7	3	Medium	Unclear
Zhang et al.[32]	1, 3	-	6	-	8	2, 4, 5, 7	3	Medium	Unclear
Stockl et al.[45]	1, 3	-	-	-	-	2, 4, 5, 6, 7, 8	2	Low	Unclear

*Methodologic quality criteria as described by Van Tulder et al.[36]; Adapted from Reininga IH, Zijlstra W, Wagenmakers R, Boerboom AL, Huijbers BP, Groothoff JW, Bulstra SK, Stevens M. Minimally invasive and computer-navigated total hip arthroplasty: a qualitative and systematic review of the literature. BMC Musculoskelet Disord 2010;11:92.

Table 2. Results of postoperative rotational alignment of components

Study	Methodologic quality	Number of patients	Femoral rotation SMD (95% CI)*	Tibial rotation SMD (95% CI)*	Tibiofemoral mismatch SMD (95% CI)*
Schmitt et al.[31]	High	47	NR	0.18 (-0.40 to 0.75)	NR
Kim et al.[39]	Medium	200	-0.47 (-0.75 to -0.19)	0.00 (-0.28 to 0.28)	NR
Lutzner et al.[37]	Medium	80	1.90 (1.37, 2.44)	-1.93 (-2.46 to -1.39)	NR
Mombert et al.[40]	Medium	42	NE (NS)	NR	NR
Blakeney et al.[18]	Medium	66	-0.19 (-0.68 to 0.29)	NR	-0.23 (-0.72 to 0.25)
Han et al.[42]	Medium	120	-0.05 (-0.58 to 0.48)	NR	NR
Matziolis et al.[9]	Medium	60	0.11 (-0.40 to 0.62)	-0.11 (-0.62 to 0.40)	NR
Zhang et al.[19]	Medium	64	0.19 (-0.30 to 0.68)	NR	NR
Carter et al.[43]	Medium	200	0.17 (-0.10 to 0.45)	0.47 (0.19-0.75)	NR
Choong et al.[14]	Medium	104	NE (NS)	NR	NR
Hiscox et al.[29]	Medium	32	0.62 (-0.09 to 1.33)	0.21 (-0.49 to 0.90)	-0.38 (-1.08 to 0.32)
Kim et al.[44]	Medium	320	-0.32 (-0.54 to -0.10)	0.41 (0.18-0.63)	NR
Zhang et al.[32]	Medium	81	-0.64 (-1.09 to -0.19)	-0.16 (-0.59 to 0.28)	-0.49 (-0.93 to -0.04)
Stockl et al.[45]	Low	64	NE (S, decrease)	NR	NE (NS)

*Negative SMD with 95% CI indicates a decrease in deviation of neutral rotation in favor of intervention group; SMD=standardized mean difference; NE=SMD not estimable; S=significant; NS=not significant; NR=not reported.

RESULTS

Conflicting evidence was found among eligible studies on the effect of imageless CAS on femoral and tibial component rotation, and moderate evidence was identified that imageless CAS does not improve tibiofemoral mismatch. Thirteen studies reported on postoperative rotation of the femoral component (Table 2). Three medium- and one low-quality study reported a significant decrease in deviation from the neutral rotation of the femoral component with use of imageless CAS. Eight medium-quality studies did not find a significant difference. One medium-quality study showed an increase in deviation from the neutral rotation of the femoral component (Fig. 2). Eight studies reported on rotation of the tibial component (Table 2). One medium-quality study reported a significant decrease in deviation from the neutral rotation of the tibial component by using imageless CAS. One high-quality study and four medium-quality studies did not find a significant difference. Two medium-quality studies found an increase in deviation (Fig. 3). Four studies reported on tibiofemoral mismatch (Table 2). None of the studies showed a significant difference. A sensitivity analysis using different cutoff points for methodologic quality also showed conflicting evidence

on the subjects of femoral and tibial rotation, and moderate evidence that imageless CAS does not improve tibiofemoral mismatch (Fig. 4).

Conflicting evidence was found regarding the effect of imageless CAS on the number of femoral and tibial outliers. The number of femoral rotational outliers was reported in 11 studies (Table 3). Two medium-quality studies found a decrease in the number of outliers, whereas seven studies of medium quality showed no significant difference. Two medium-quality studies found a significant increase in the number of femoral rotational outliers (Fig. 5). The number of tibial rotational outliers was compared in seven studies (Table 3). One study of medium methodologic quality showed a significant decrease. No significant difference between the two groups was found in one high-quality and four medium-quality studies. One medium-quality study reported a significant increase in the number of tibial outliers (Fig. 6). A sensitivity analysis also showed conflicting evidence regarding the effect of imageless CAS on the number of femoral and tibial outliers.

	CAS			Conventional				Std. Mean Difference	Std. Mean Difference
Study or Subgroup	Mean	SD	Total	Mean	SD	Total	Weight	IV, Fixed, 95% CI	IV, Fixed, 95% CI
Blakeney et al.[18]	1.18	1.22	34	1.44	1.44	32	5.9%	-0.19 [-0.68, 0.29]	
Carter et al.[43]	1.21	2	100	0.87	1.9	100	17.9%	0.17 [-0.10, 0.45]	
Han et al.[42]	2.05	2.53	27	2.17	2.31	28	4.9%	-0.05 [-0.58, 0.48]	
Hiscox et al.[29]	2.06	3.05	17	0.04	3.33	15	2.7%	0.62 [-0.09, 1.33]	
Kim et al.[44]	0.5	1.2	160	0.9	1.3	160	28.3%	-0.32 [-0.54, -0.10]	
Kim et al.[39]	-2	2.27	100	-1	1.93	100	17.4%	-0.47 [-0.75, -0.19]	
Lutzner et al.[37]	1.08	1.75	40	-11.75	9.27	40	4.9%	1.90 [1.37, 2.44]	
Matziolis et al.[9]	0.3	1.4	32	0.1	2.2	28	5.3%	0.11 [-0.40, 0.62]	
Zhang et al.[19]	1.3	3.27	32	0.7	2.97	32	5.7%	0.19 [-0.30, 0.68]	
Zhang et al.[32]	-0.63	3.04	40	1.51	3.55	41	6.9%	-0.64 [-1.09, -0.19]	
Total (95% CI)			**582**			**576**	**100.0%**	**-0.07 [-0.19, 0.04]**	

Heterogeneity: Chi² = 80.19, df = 9 (P < 0.00001); I² = 89%
Test for overall effect: Z = 1.23 (P = 0.22)

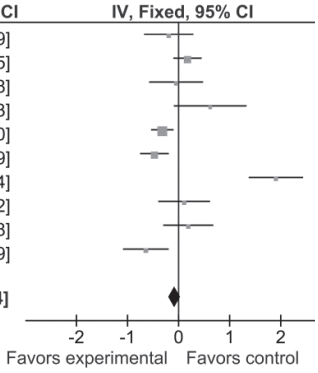

Figure 2. The forest plot compares imageless CAS TKA with conventional TKA in terms of femoral rotation. CAS=computer-assisted surgery; Std=Standardized; IV=Inverse Variance; df=degrees of freedom.

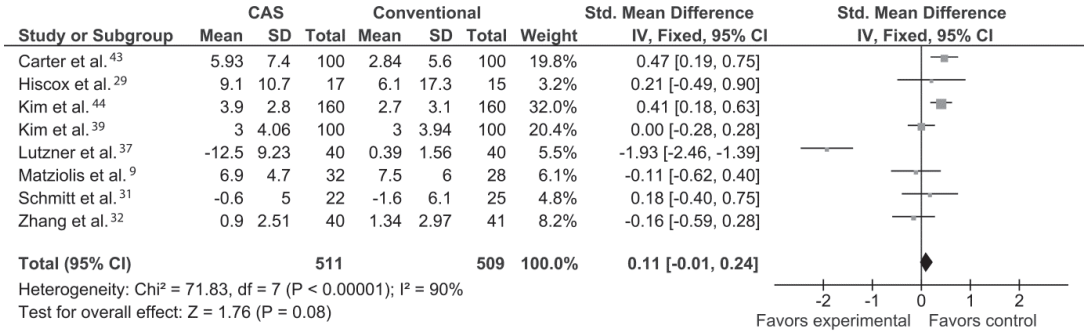

Figure 3. A comparison of tibial rotation for imageless CAS TKA and conventional TKA is shown. CAS=computer-assisted surgery; Std=Standardized; IV=Inverse Variance; df=degrees of freedom.

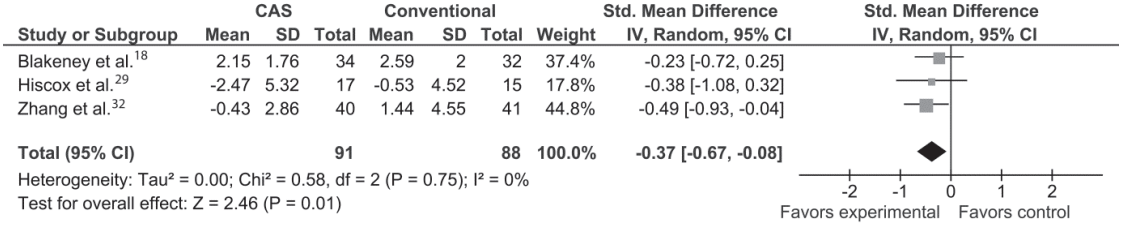

Figure 4. Imageless CAS TKA was compared with conventional TKA for tibiofemoral mismatch. CAS=computer-assisted surgery; Std=Standardized; IV=Inverse Variance; df=degrees of freedom.

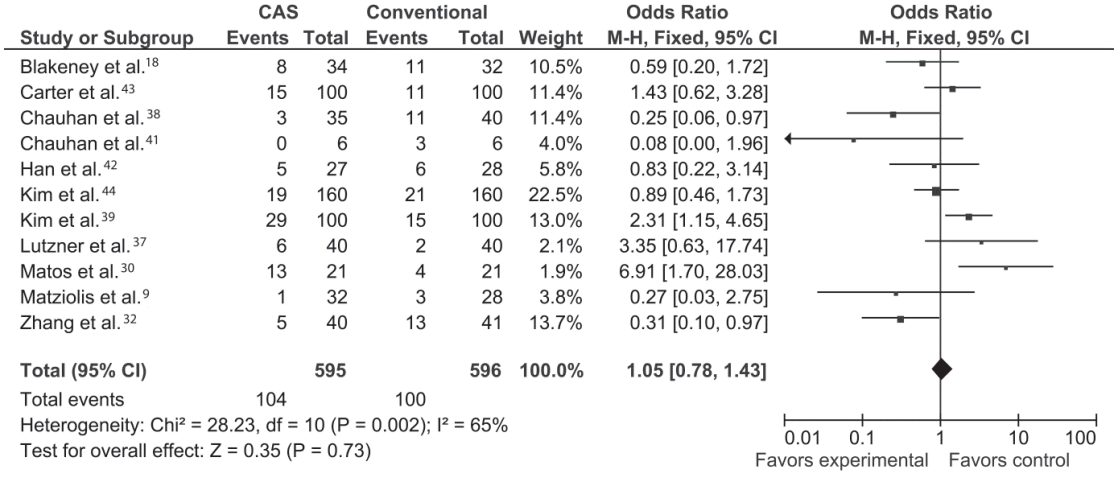

Figure 5. A comparison of femoral rotational outliers for CAS TKA and conventional TKA is shown in this forest plot. CAS=computer-assisted surgery; M-H=Mantel-Haenszel; df=degrees of freedom.

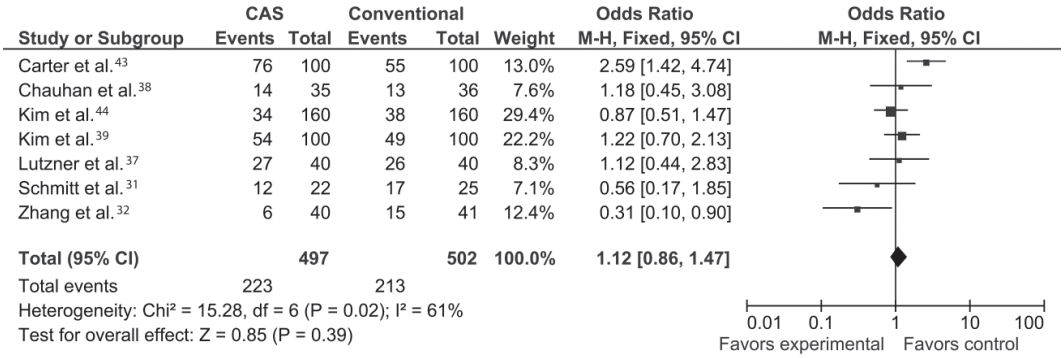

Figure 6. A comparison of imageless CAS TKA and conventional TKA for the number of tibial rotational outliers is shown. CAS=computer-assisted surgery; M-H=Mantel-Haenszel; df=degrees of freedom.

Table 3. Rotational outliers

Study	Methodologic quality	Number of outliers femur			Number of outliers tibia		
		Study group	Control group	OR (95% CI)*	Study group	Control group	OR (95% CI)*
Schmitt et al.[31]	High	NR	NR	NR	12/22	17/25	0.56 (0.17-1.85)
Matos et al.[30]	Medium	13/21	4/21	6.91 (1.70-28.03)	NR	NR	NR
Chauhan et al.[38]	Medium	3/35	11/40	0.25 (0.06-0.97)	14/35	13/36	1.18 (0.45-3.08)
Kim et al.[39]	Medium	29/100	15/100	2.31 (1.15-4.65)	54/100	49/100	1.22 (0.70-2.13)
Lützner et al.[37]	Medium	6/40	2/40	3.35 (0.63-17.74)	27/40	26/40	1.12 (0.44-2.83)
Blakeney et al.[18]	Medium	8/34	11/32	0.59 (0.20-1.72)	NR	NR	NR
Chauhan et al.[41]	Medium	0/6	3/6	0.08 (0.00-1.96)	NR	NR	NR
Han et al.[42]	Medium	5/27	6/28	0.83 (0.22-3.14)	NR	NR	NR
Matziolis et al.[9]	Medium	1/32	3/28	0.27 (0.03-2.75)	NR	NR	NR
Carter et al.[43]	Medium	15/100	11/100	1.43 (0.62-3.28)	76/100	55/100	2.59 (1.42-4.74)
Kim et al.[44]	Medium	19/160	21/160	0.89 (0.46-1.73)	34/160	38/160	0.87 (0.51-1.47)
Zhang et al.[32]	Medium	5/40	13/41	0.31 (0.10-0.97)	6/40	15/41	0.31 (0.10-0.90)

*An OR less than 1 with 95% CI indicates lower odds outliers in favor of the intervention group; OR=odds ratio, NR=not reported.

DISCUSSION

The use of imageless CAS during TKA has been shown to improve coronal and sagittal knee prosthetic alignment.[16-20] However, whether imageless computer navigation influences rotational alignment was unclear. Our aim therefore was to review the literature evaluating the effectiveness of imageless CAS during TKA on rotational alignment of the femoral and tibial components and tibiofemoral mismatch and the number of femoral and tibial rotational

outliers. The results of this systematic review showed no evidence that a TKA with imageless CAS leads to better rotational alignment of the femoral or tibial component or tibiofemoral mismatch. Furthermore, no evidence was found that imageless CAS results in a decrease of the number of outliers in terms of femoral or tibial component orientation.

Our study has some limitations. First, only studies published in English, Dutch, German, French, or Spanish were included. This may have led to selection bias. However, we excluded only two studies based on language. Therefore we expect that this selection procedure had minimal influence on selection bias. Second, only studies using imageless navigation were included. There are two different techniques in CAS: image-based and imageless computer navigation. With a CAS TKA, imageless navigation is used mostly in daily practice. Therefore, we included only studies in which an imageless navigation system was used.

In addition to coronal and sagittal prosthetic alignment, only one narrative review by Burnett and Barrack[25] took into account femoral and tibial rotational alignment. They concluded that use of imageless CAS during TKA did not improve femoral or tibial rotational alignment. However, methodologic quality of the studies was not taken into account and they did not perform a statistical analysis. Moreover, the number of included studies was low (nine studies). Our systematic review confirms that TKA with imageless CAS does not improve femoral or tibial rotational alignment. To our knowledge, our systematic review is the first to analyze the effect of imageless CAS on postoperative tibiofemoral mismatch and we did not find an improvement for this outcome either. We assessed whether the sample size calculation of the included studies was based on one of the outcome measures used in this systematic review. This was the case for only one study reporting femoral and tibial rotational alignment.[37] It is possible that the included studies failed to have sufficient power to assess significant differences in these outcome measures. No gold standard exists for determining rotational alignment of the tibial component. Five different measurement protocols were used in the included studies. The protocol of Berger et al.[10] (center of proximal tibial plateau relative to the tip of the tubercle) was used in three studies,[29,32,43]

that of Matziolis et al.[9] (tibial fins relative to the line between the medial third of the tubercle and the geometric center of gravity of the tibia) in three studies,[9,37,44] and the Perth protocol[41] (posterior tibial condyles relative to the tuberosity) in one study.[38] Tibial component rotation relative to the ankle was used in one study,[31] and tibial component rotation relative to the posterior border of the proximal tibia also was used in one study.[39] These protocols use different anatomic landmarks to assess rotational tibial alignment; therefore, results of the influence of imageless CAS in tibial rotational alignment should be interpreted with caution because no gold standard for this measurement exists. In clinical practice, rotational alignment of the femoral component generally is measured relative to the epicondylar axis[34]; therefore, three studies in which this was not the case were excluded.

One narrative review[25] and two systematic reviews[26,27] evaluated the effect of TKA with imageless CAS on the number of postoperative femoral and tibial rotational outliers. The conclusion of these reviews was that TKA using imageless CAS did not decrease the number of tibial and femoral rotational outliers.[26,27] The number of studies included in the three reviews was low, methodologic quality was not taken into account, and strong heterogeneity existed. Our systematic review confirms the results of the previous reviews that TKA with imageless CAS does not decrease the number of femoral or tibial rotation rotational outliers. The sample size calculation was based on one of the outcome measures in only one study, thus the included studies in this systematic review may be underpowered. To include as many studies as possible, we used a broad search strategy. In contrast with previous systematic reviews,[26,27] clinical controlled trials and cadaveric studies also were included. As a result, we included 17 studies in total, whereas a maximum of six studies was included in previous systematic reviews.[26,27] Including studies other than RCTs or Level I studies may provide important information or can be of high reporting quality.[28,47] Because no gold standard exists for measuring tibial rotation, five different measurement protocols were used in the included studies. Therefore, results of the influence of imageless CAS in tibial rotational alignment should be interpreted with caution. Three studies in which femoral rotation was not measured relative to the epicondylar axis, were excluded.

Results of our systematic review show no evidence that TKA with imageless CAS leads to better rotational alignment of the femoral or tibial component or tibiofemoral mismatch. No evidence was found that imageless CAS results in a decrease of the number of outliers in terms of femoral or tibial component orientation. To our knowledge, this is the first review to systematically analyze the influence of imageless CAS on postoperative deviation of prosthetic components from the neutral rotational axis. Previous reviews did not take into account the methodologic quality or sample size calculation of the included studies. In addition, to our knowledge, the effect on tibiofemoral mismatch has not been described before. Even so, these conclusions should be interpreted with caution. The number of included studies was low, only one of the 17 included studies was considered of high methodologic quality, and different methods for assessing tibial component rotation were used in the studies. The sample size calculation was based on one of the outcome measures in only one of the included studies. To gain more insight into the effect of TKA with imageless CAS on rotational alignment, a systematic review should be performed that includes more studies and of high methodologic quality with sample size calculations based on one of the outcome measures. The outcome measures have to be measured using the same measurement protocol.

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CONFLICT OF INTEREST

Each author certifies that he or she, or a member of his or her immediate family, has no funding or commercial associations (eg, consultancies, stockownership, equity interest, patent/licensing arrangements, etc) that might pose a conflict of interest in connection with the submitted article.

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Chapter 9

Computer-assisted revision TKA: the effect on postoperative knee prosthesis alignment

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ABSTRACT

Introduction: The use of computer-assisted surgery (CAS) during primary total knee arthroplasty (TKA) is known to improve knee prosthesis alignment. However, literature on the use of CAS during revision TKA (rTKA) is scarce. Moreover, the effect of CAS-rTKA on rotational alignment has not been described yet. Purpose of this study was therefore to investigate whether CAS-rTKA improves coronal, sagittal and rotational knee prosthesis alignment and reduces the number of outliers compared to the conventional technique.

Materials and methods: A prospective clinical intervention study (CAS-rTKA) with use of a historical control group (CON-rTKA) was conducted. The CAS-rTKA group included 29 patients (31 knees) who underwent rTKA using imageless CAS between January 2012 and January 2015, and the CON-rTKA group included 23 patients who were operated using the conventional technique between January 2002 and January 2012. Postoperative alignment was measured using the EOS 2D/3D system (coronal and sagittal planes) and CT-scan (rotation).

Results: There were no significant differences in coronal and sagittal alignment measurements and femoral rotation. There was a significant difference in rotation of the tibial plateau in the CAS-rTKA group, showing relatively more internal rotation than the CON-rTKA group (P=0.004). No significant differences were seen in the proportions of coronal, sagittal or rotational outliers.

Conclusions: This study showed no evidence that the use of CAS during revision TKA leads to improved coronal, sagittal or rotational alignment of a knee prosthesis or fewer outliers. The tibial component had a more internally rotated placement with the use of CAS, but the proportion of outliers for this measurement was comparable for both groups. The findings of this study should be interpreted with caution, as the number of included patients was low.

INTRODUCTION

Due to an increase of primary total knee arthroplasties (TKAs)[1] and longer survival of both prosthesis and patient, a dramatic increase in the number of revision TKA (rTKA) is predicted for the coming years.[2] Compared to primary TKA, rTKA is a more complicated procedure due to extensive bone loss and ligamental damage[3,4] and results in worse clinical results and shorter survival.[5-7] Due to bone deficits and thus disappearance of anatomical landmarks, it is a challenge to determine the right prosthetic position. Achieving optimal prosthetic alignment during rTKA is essential, as malalignment leads to earlier aseptic loosening while ranking as second most frequent mode of failure after rTKA.[8,9]

Computer-assisted surgery (CAS) has been developed to enhance prosthetic alignment. In primary TKA, CAS has proven to be a very useful technique. The use of CAS in primary TKA results in improved postoperative alignment of the knee prosthesis with fewer outliers, compared to conventional techniques. Multiple studies have shown a better coronal and sagittal postoperative alignment after primary TKA with use of CAS, compared to conventional TKA.[10-16] Whether CAS also improves rotational alignment is still a matter of debate though.[17] Studies on the application of CAS in rTKA are rare. De Ladoucette et al.[18] reported on the results of 15 rTKAs with use of CAS (CAS-rTKA). They concluded that CAS is a useful technique for aligning the knee prosthesis in the frontal plane. Thielemann et al.[19] and Sikorski et al.[20] confirmed these findings with their experience in respectively 46 and 14 cases. In a retrospective study conducted by Jenny et al.[21] the postoperative alignment of 50 CAS-rTKAs was compared with 36 conventional TKAs. They found a significant improvement in optimal global implantation in the navigated group. In a prospective study by Perlick et al.[22] the results of 25 CAS-rTKAs were compared with those of 25 conventional rTKAs. Both the mechanical axis and the coronal orientation of the femoral component, placed while using CAS, were superior and had fewer outliers than the conventional technique. Moreover, CAS allows the surgeon to verify and document prosthetic alignment, range of motion, ligamental situation and bone resection during surgery, making it a very useful technique during this complicated procedure.[22]

Although these few studies do indicate that CAS improves prosthetic alignment in rTKA, the study groups are small and only two studies[21,22] compare the results with conventional rTKA. Moreover, no study has analyzed the effect of CAS on rotational alignment yet. Hence the aim of this study is to investigate the effect of the use of CAS during rTKA, not only on coronal and sagittal but also on rotational prosthetic alignment. Results will be compared with a historical control group in which rTKA was performed without CAS.

MATERIALS AND METHODS

Study design

A prospective clinical intervention study with use of a historical control group was conducted at the Department of Orthopedics of University Medical Center Groningen. Patients who underwent rTKA between January 2012 and January 2015 using an imageless CAS system were included in the intervention group. The historical control group consisted of patients who underwent rTKA without the use of CAS between January 2002 and January 2012. The study design is extensively described elsewhere[23] and has been approved by the Medical Research Ethics Committee of University Medical Center Groningen (UMCG).

Study population

Inclusion criteria for both the intervention group and the historical control group were:

- Use of imageless CAS during rTKA for the intervention group and use of conventional alignment guides during rTKA for the historical control group;
- Minimum age of 18 years;
- A total or partial revision of either the tibial or the femoral part was performed. For partial revisions, only measurements of the part of the prosthesis to be revised were used.

Exclusion criteria were:

- Insert replacements and placement of a patellar button only;
- Placement of a tumor prosthesis during rTKA;
- Placement of a Rotating Hinge Knee prosthesis;
- Revision because of an infected knee prosthesis;
- A limited knowledge of the Dutch language or mental incapacity to participate in the study.

In both groups the anesthetic, analgesic and postoperative physiotherapeutic protocols were identical. Demographic characteristics, BMI, indication for operation, type of prosthesis, surgical time and length of hospital stay were collected and/or recorded for all patients included in this study.

Surgical procedure rTKA

Revision TKA consisted of three steps: 1) removal of implant, 2) classification of defects and 3) rebuilding of the knee joint by preparing the tibia first. The first step was to extract the failing components and to remove all debris. Bone was preserved as much as possible, although bone of poor quality had to be removed. The second step was to classify the bone defects according to the Anderson Orthopaedic Research Institute (AORI).[24] In defect types 2A, 2B and 3 bone loss was compensated by metal augmentations, while stems attached to the tibial and femoral components spread the load to the implant interfaces to secure fixation. The third step was rebuilding of the knee joint with a revision prosthesis. The NexGen® Legacy Condylar Constraint Knee® (LCCK) revision system (Zimmer Inc., Warsaw, Indiana, USA) was used, placing tibial and femoral revision components with press-fit stems and, if needed, with augmentation blocks or trabecular metal cones. The prosthesis was fixed with bone cement (Refobacin® revision bone cement with clindamycin and gentamicin, Biomet Inc., Warsaw, Indiana, USA). Depending on the stability and integrity of the collateral ligaments a choice was made during surgery for type of articulating surface. A posterior stabilizing component

(Legacy Posterior Stabilized®, LPS) was used for good collateral ligaments, and a semi-constraint insert (LCCK) with a high post in case of coronal plane instability.

Intervention group

Imageless CAS was applied during rTKA in the intervention group, using the ORTHOsoft Navitrack® navigation system (Zimmer Inc., Warsaw, Indiana, USA). The navigation is based on an infrared reflecting system with use of trackers on the femur and tibia. The system guides the surgeon by an image-free model based on anatomical landmarks identified by the surgeon. After exposure a femoral tracker was placed proximally from the knee in the same knee wound. The tibial tracker was placed in an additional 3-cm incision above the ankle. Before removal of the primary prosthesis, a navigation protocol was followed in which the anatomical landmarks are chosen and the system builds its model from the patient's data. All anatomical landmarks were thus identified with the primary prosthesis in situ. The mechanical axis of the lower limb as measured with the navigation system was the angle between the mechanical axis of the femur and tibia. The mechanical axis of the femur was the axis between the center of the femoral head and the distal entry point of the medullary canal. The center of the femoral head was determined by moving the leg in a conical pattern, digitizing 14 distinct positions of the femoral tracker. The entry point of the distal medullary canal was marked by the orthopedic surgeon. The mechanical axis of the tibia was the axis between the proximal entry point of the medullary canal and the center of the ankle. The entry point of the medullary canal was marked by the orthopedic surgeon and the center of the ankle was assessed by marking the medial and lateral malleoli. Coronal and sagittal prosthetic alignment of the femoral and tibial components was calculated according to respectively the femoral and tibial mechanical axes. Rotation of the femoral component was determined according to the epicondylar axis. The orthopedic surgeon marked the medial and lateral epicondyles to generate this axis. Rotation of the tibial component was assessed in relation to the axis between the middle

of the posterior cruciate ligament insertion and the medial third of the tibial tuberosity. Both landmarks were marked by the orthopedic surgeon. The navigation system guided the surgeon in positioning the components and determining the size of the implants.

When implanting a press-fit stem, alignment of the components could be influenced by the stem. After removal of the primary prosthesis and preparation of the bone cuts, various provisional components were tried in order to determine their correct type and size. In this way, and by checking component alignment with the navigation system, the orthopedic surgeon knew if the stem influenced the component alignment. In the revision system we had the availability of straight stems and off-set stems to rebuild the best position of the component in combination with the stem but not forced by the stem. When this was the case, an undersized stem was chosen so that the components were placed according to the bone cut made using the navigation system instead of indication by the stem.

Historical control group

In the control group the position of the revision prosthesis was determined using NexGen® mechanical intramedullary alignment guides for the femur and tibia (Zimmer Inc., Warsaw, Indiana, USA). Positioning of the components and sizing were based on the same anatomical landmarks as in the intervention group, with use of prototypes and trial components.

Radiographic evaluation of prosthesis alignment

To evaluate alignment in the coronal and sagittal planes a new imaging device, the EOS 2D/3D system (EOS Imaging, Paris, France),[25] was used. This device is characterized by lower radiation (800-1000 times less than CT-scan and one-tenth of conventional X-ray).[25,26] The EOS imaging device uses two orthogonal sources of radiation and linear detectors that are coupled together. These sources move up and down along the patient, producing coronal and sagittal images simultaneously while the patient is in weight

bearing position. This is a different technique than conventional radiograph systems, where beams are divergent in the horizontal and vertical planes. EOS images were used to measure prosthetic alignment in both the intervention and the historical control group. For both groups, standard coronal and sagittal X-rays were taken postoperatively as part of the standard operation protocol. The measurements were performed by one person (MFM) who had extensive experience in taking EOS 2D and 3D measurements before the start of this study.

Angles measured for coronal and sagittal alignment were:

- Mechanical angle of the leg (HKA): Angle between the line from the femoral head to the center of the knee and the line from the center of the ankle to the center of the knee in the coronal plane. The HKA was measured in 3D using the sterEOS software (EOS Imaging, Paris, France) and according to the measurement protocol as described earlier.[27]

- Mechanical lateral distal femoral angle (mLDFA): Angle between the mechanical axis of the femur and the articular surface of the femoral part of the prosthesis in the coronal plane. The mLDFA was measured in 2D, as 3D measurements were not possible with the sterEOS software.

- Mechanical medial proximal tibial angle (mMPTA): Angle between the mechanical axis of the tibia and the articular surface of the tibial part of the prosthesis in the coronal plane. The mMPTA was measured in 2D, as 3D measurements were not possible with the sterEOS software.

- Anatomical proximal posterior tibial angle (aPPTA): Angle between the mechanical axis of the tibia and the articular surface of the tibial part of the prosthesis in the sagittal plane. The aPPTA was measured in 2D, as 3D measurements were not possible with the sterEOS software used. Downslope of the design of Nexgen prostheses is 7˚; this angle is considered the normal aPPTA.

For the mechanical axis of the leg, mLDFA, mMPTA and aPPTA a generally accepted outlier cut-off of ±3° was applied in this study.[28,31]

The canal-filling ratio (CFR) was determined in both the intervention

and control groups to assess whether the stems were filling the medullary canal. The CFR was measured on the coronal EOS images as described by Parsley et al.[32] Stem and endosteal diameters were measured at the stem tip. CFR was calculated by dividing the stem diameter by the endosteal diameter. A stem was considered to be canal-filling when the CFR was ≥0.85.[32]

Rotational prosthetic alignment was measured on a CT-scan of the operated leg. Of the patients in the intervention group, a CT-scan of the operated leg was made postoperatively during the clinical follow-up visits at the outpatient clinic. Patients in the historical control group were invited to our hospital for an appointment, during which a CT-scan was made.

For evaluation of rotational prosthetic alignment, rotation of the femoral component was determined according to the Berger CT protocol.[33] The CT-scans were anonymized by removing names and patient numbers. The measurements were performed blindly by an orthopedic surgeon (ALB) who had extensive experience doing this. Angles measured for rotational alignment were:

- Condylar twist angle for rotation of the femoral component: angle between the epicondylar axis and the prosthetic posterior condylar axis (inner border of posterior cut). External rotation of the femoral component is shown as a positive (+) angle and internal rotation of the femoral component is shown as a negative (-) angle. An angle >3˚ internal rotation or external rotation is considered an outlier.[34,36]

- Rotation of the tibial component: the line perpendicular to the posterior border of the tibial plateau is measured relative to the projection of the tuberosity (Fig. 1). Neutral alignment is considered 0˚. External rotation of the tibial component is shown as a positive (+) angle and internal rotation of the tibial component is shown as a negative (-) angle. An angle >3˚ endorotation or exorotation is considered an outlier.[34,35,37]

Sample size

The hypothesis was that the use of CAS leads to fewer outliers in prosthetic

alignment than the use of mechanical alignment guides during rTKA. Primary outcome measure was rotational prosthetic alignment. When using the conventional operation technique, around 25% of the knees are considered radiological outliers.[16,38] Previous research has shown that the use of CAS in TKA decreases the number of outliers by 17-30%.[16,39,40] We expected a 20% decrease in outliers in the CAS group compared to the historical control group. Hence with a P1 of 0.95, P2 of 0.75, alpha of 0.05 and a power of 80%, 44 knees per group were needed. In the end, 31 knees operated on between January 2012 and January 2015 were included in the intervention group and 23 knees operated on between January 2002 in January 2012 were included in the historical control group, which means that the study is underpowered.

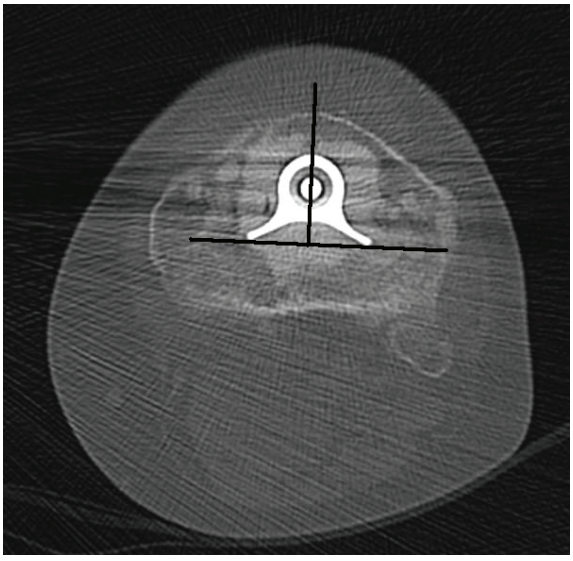

Figure 1. The line perpendicular to the posterior border of the tibial plateau relative to the projection of the tuberosity represents the rotation of the tibial component.

Statistical analysis

All statistical analyses were performed using IBM SPSS Statistics for Windows software (Version 22.0, Armonk, NY: IBM Corp.). Descriptive statistics were used to describe the main characteristics of the two research groups. For the clinical parameters, t-tests were used for continuous values or the

Mann-Whitney U-test when the variables were not normally distributed. Differences in rotational, coronal and sagittal alignment between the groups were determined by using the nonparametric Mann-Whitney U-test for independent samples. A Chi-square test and a Fisher's Exact test were used for dichotomous values. For all test procedures, a p-value <.05 was considered to indicate statistical significance.

RESULTS

A total of 54 knees (50 patients) were included in this study (Fig. 2). The intervention group (CAS-rTKA) included 29 patients (31 knees) and the historical control group (CON-rTKA) 23 patients. Two patients were allocated to the CAS-rTKA group with one knee and to the CON-rTKA group with the other knee. Patient demographics and characteristics are presented in Table 1 and were equal between the two groups. Operation time for total and partial revisions and length of hospital stay did not show significant differences between the two groups (Table 1). Main indications for revision in this study were aseptic loosening (22 cases), malpositioning (15 cases) and instability (10 cases).

In the CAS-rTKA group, the HKA could not be measured in 3D in two cases due to a technical error of the software, leaving 20 knees available for HKA measurements. In four cases the medial and/or lateral epicondyle was not visible on the CT-scan, leaving 19 knees available for measurement of femoral rotation. In two cases, rotation of the tibial component could not be measured because the tuberosity was not visible on CT-scan, leaving 26 knees available for evaluation of tibial rotational alignment. In the CON-rTKA group, the medial and/or lateral epicondyle was not visible on the CT-scan in three cases, leaving 14 knees available for evaluation of femoral rotation. In four cases the tuberosity was not visible on CT-scan, leaving 17 knees available for evaluation of tibial rotation (Table 2).

Table 1. Patient demographics and characteristics.

	CAS-rTKA	CON-rTKA	P-value
Number of knees (M/F)	31 (13/18)	23 (12/11)	
Number of total revisions	22	19	
Number of partial revisions	9	4	
Age* (years)	62 (28)	60 (50)	0.43
Body Mass Index**	30 (4.9)	30 (5.6)	0.94
Operation time total revisions (minutes)**	243 (147)	261 (155)	0.41
Operation time partial revisions (minutes)**	150 (114)	166 (93)	0.94
Length of hospital stay**	8 (8)	8 (9)	0.34

Abbreviations: M=male; F=female; CAS-rTKA=intervention group on which computer-assisted surgery is used during revision total knee arthroplasty; CON-rTKA=historical control group on which the conventional technique is used during revision total knee arthroplasty.
*Values are given as median and range
**Values are given as mean ± standard deviation

Table 2. Postoperative alignment angles for the CAS-rTKA and CON-rTKA group.

Alignment angle	N	CAS-rTKA	N	CON-rTKA	P-value
Median HKA (range)	20	0.3 (11.4)	19	-1.1 (9.0)	0.13
Median mLDFA (range)	24	0.3 (8.9)	19	0.0 (14.1)	0.50
Median mMPTA (range)	29	0.0 (11.5)	23	0.0 (4.8)	0.64
Median aPPTA (range)	29	4.2 (10.1)	23	4.9 (7.7)	0.12
Median rotation femur (range)	19	-1.0 (8.0)	14	-0.5 (13)	0.93
Median rotation tibia (range)	26	-2.0 (43)	17	4.0 (28)	0.004*

Medians and ranges are displayed in degrees (°).
Abbreviations: HKA=mechanical angle of the leg; mLDFA=mechanical lateral distal-femoral angle; mMPTA=mechanical medial proximal tibial angle; aPPTA=anatomical proximal posterior tibial angle; CAS-rTKA=intervention group in which computer-assisted surgery is used during revision total knee arthroplasty; CON-rTKA=historical control group in which the conventional technique is used during revision total knee arthroplasty.
An * indicates statistical significance (P <.05)

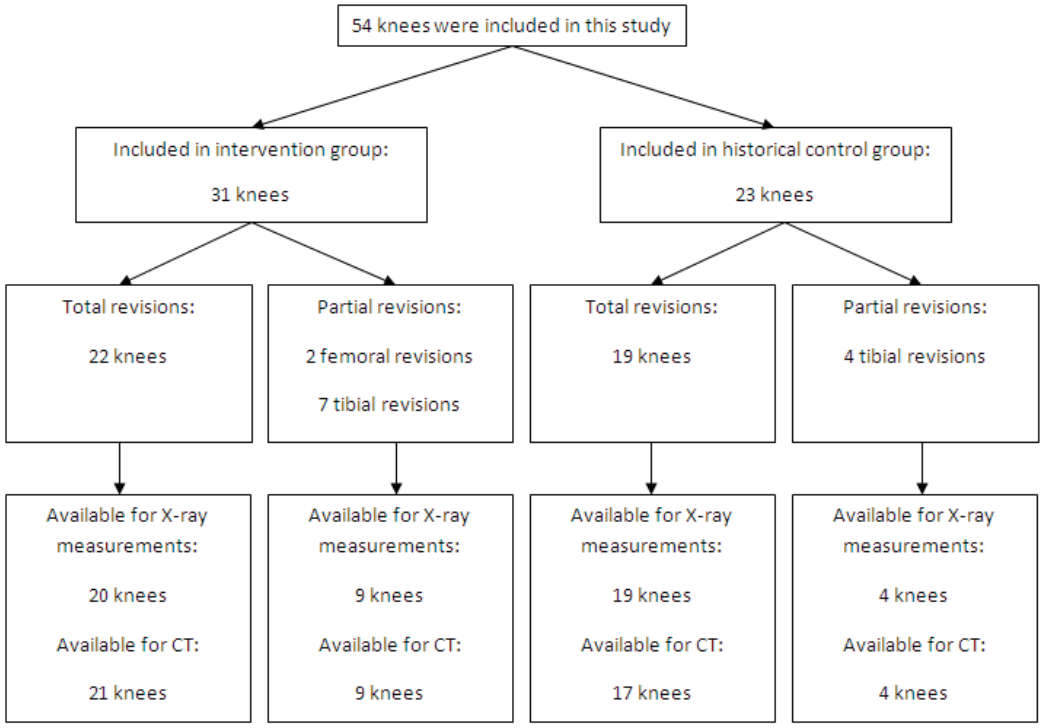

Figure 2. Flow chart of the included patients.

Table 3. Distribution of outliers for different alignment angles for the CAS-rTKA and CON-rTKA group.

Alignment angle	Amount of outliers / no outliers CAS-rTKA	Amount of outliers / no outliers CON-rTKA	P-value*
HKA	3 / 17	5 / 14	0.38
mLDFA	4 / 20	4 / 15	0.71
mMPTA	5 / 24	1 / 22	0.15
aPPTA	12 / 17	6 / 17	0.25
Rotation femur	2 / 17	3 / 11	0.39
Rotation tibia	11 / 15	10 / 7	0.29

Abbreviations: HKA=mechanical angle of the leg; mLDFA=mechanical lateral distal-femoral angle; mMPTA=mechanical medial proximal tibial angle; aPPTA=anatomical proximal posterior tibial angle; CAS-rTKA=intervention group in which computer-assisted surgery is used during revision total knee arthroplasty; CON-rTKA=historical control group in which the conventional technique is used during revision total knee arthroplasty.
*Chi-square test

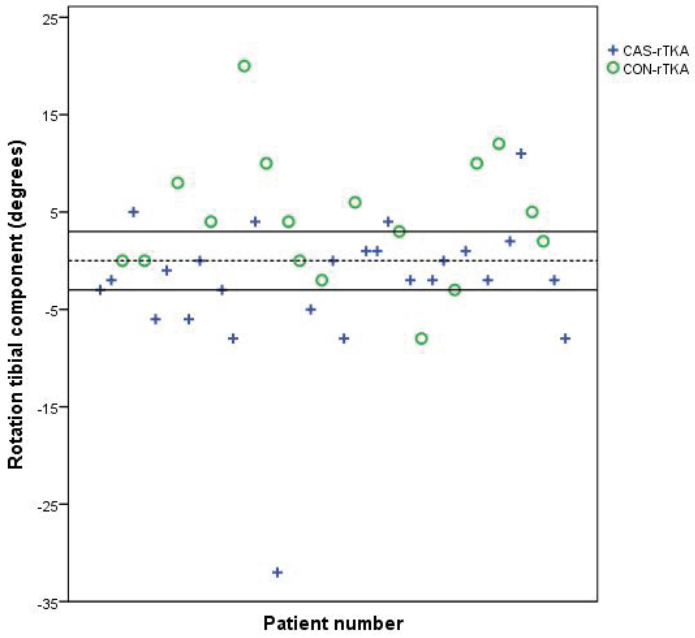

Figure 3. Tibial components of the CAS-rTKA group are more internally rotated compared to the CON-rTKA group. The black lines mark the safe zone (+/-3 degrees) and the dotted line represents the neutral orientation.

Alignment measurements

The coronal and sagittal alignment measurements and femoral rotation did not differ significantly between the two groups. However, there was a significant difference between the rotation of the tibial plateau, with the CAS-rTKA groups showing relatively more internal rotation than the CON-rTKA group (P=0.004) (Table 2) (Fig. 3). For the proportions of coronal, sagittal and rotational outliers there were no significant differences between the CAS-rTKA and the CON-rTKA group (Table 3).

Canal-filling ratio

In the CAS-rTKA group 24 femoral components were implanted with a stem; six of them were canal-filling. In the CON-rTKA group 19 femoral components were implanted with a stem, and four of them were canal-filling. The proportion of canal-filling femoral stems did not differ significantly between the two groups (P=0.76). In the CAS-rTKA group 12 of the 28 implanted tibial

stems were considered canal-filling, whereas in the CON-rTKA group seven out of 22 were considered canal-filling. Again, the proportion of canal filling stems did not differ significantly between the groups (P=0.43).

DISCUSSION

The use of CAS in primary TKA is known to improve postoperative knee prosthesis alignment. However, literature on the use of CAS during revision TKA is limited. The study groups were small and only two studies have compared the results after CAS-rTKA with the conventional technique. Moreover, the effect of CAS-rTKA on rotational alignment has not been investigated yet. Purpose of this study was therefore to investigate whether CAS-rTKA improves coronal, sagittal and rotational knee prosthesis alignment compared to the conventional technique.

Coronal and sagittal alignment were not improved by the use of CAS in this study. Rotational alignment of the femoral component was not significantly different between the two groups either. Placement of the tibial component, however, was more internally rotated when using CAS, while placement of the component with the conventional technique was more externally rotated. The proportion of outliers for coronal, sagittal or rotational alignment measurements did not differ between the groups.

Two other studies report on the influence of CAS-rTKA on coronal and sagittal alignment compared to the conventional technique. Jenny et al.[21] found no improvement of the HKA, mLDFA, mMPTA or aPPTA when CAS was used during rTKA, and no differences in the proportion of outliers with respect to the HKA, mLDFA, mMPTA or aPPTA. Perlick et al.[22] did find a significant improvement in HKA and mLDFA when CAS was used. Alignment of the tibial component in the coronal and sagittal planes was not significantly improved in this study. We reported the proportions of outliers but did not test whether it differed significantly between the two groups. In the study of Jenny et al.[21] 50 CAS-rTKAs were compared to 36 CON-rTKAs; they did not exclude

infections (32 cases), as a result of which the study groups were not fully comparable to the groups from our study or that of Perlick et al.[22] Moreover, no power analysis was performed in either of those studies. We did perform a power analysis, but were not able to bring in enough patients during the inclusion period. The three studies are thus potentially underpowered, which may be a reason for non-significant differences as well as differences in results between the studies.

The influence of CAS-rTKA on rotational alignment has not been reported before, although rotational alignment after primary TKA with CAS has been reported in several studies. In a systematic review performed by Meijer et al.[17] it was concluded that there is no current evidence that CAS improves rotational alignment of either the femoral or the tibial component or that there are fewer outliers, but these conclusions should be interpreted with caution. The number of available studies was low, the studies differed in methodological quality, different methods for assessing rotation of the tibial component were used, and in only one of the included studies was the power analysis based on rotational alignment.[17] In our study there was a significant difference in rotational orientation of the tibial component. It can be questioned whether this difference in orientation is of clinical importance, since the distribution of outliers is the same. No gold standard exists to measure rotation of the tibial component after TKA. References used for measurements include the tip and medial third of the tuberosity,[15,33,41] ankle[37] and posterior border of the proximal tibia.[34] In this study, the posterior border of the tibial plateau was measured relative to the projection of the tibial tuberosity. It was decided to perform the CT-measurements this way because the goal during rTKA is to align the tibial component relative to the tuberosity. Since it was not possible to identify the tuberosity in six cases, rotational alignment of the tibial component of only 26 CAS-rTKAs was compared with 17 CON-rTKAs. Due to the low number of measurements, a dearth of significant differences in number of outliers and the lack of a gold standard for this measurement, the significant difference found for rotational

alignment of the tibial component in this study must be interpreted with caution.

Coronal and sagittal measurements were performed using the EOS 2D/3D stereoradiography system.[25] Of the measurements performed, the HKA was measured in 3D using sterEOS software (EOS Imaging, Paris, France) and according to the measurement protocol as described by Meijer et al.[27] It is known that 2D HKA measurements are influenced by the position of a lower limb during acquisition. Varus/valgus angle as well as rotation and flexion of the lower limb influence 2D HKA measurements.[42-45] EOS 3D HKA measurements have proven to be more valid than 2D HKA measurements.[46,47] Moreover, these measurements have excellent intraobserver and interobserver reliability.[27] It was therefore decided to perform HKA measurements in 3D instead of 2D, as was done in previous CAS-rTKA studies. The other coronal and sagittal measurements are performed on 2D EOS images, as these measurements are not possible with the software and are thus comparable to other CAS-rTKA studies.

A frequently described disadvantage of the use of CAS during primary TKA is prolonged operation time, ranging from 8-63 minutes, and is caused by additional computer processing, pin and tracker placement, array registering of data points, and analysis of intraoperative data.[48,49] Perlick et al.[22] found an increase in operation time of 16 minutes when CAS was used during rTKA, but statistical analysis was not performed. The authors stated that in the future additional time might be further reduced by improving the navigation workflow and developing navigation-adapted instruments.[22] In this study, median operation time was 18 and 16 minutes shorter in the CAS-rTKA group for respectively total and partial revisions, yet these differences were not statistically significant. The orthopedic surgeons who performed the operations found CAS to be a helpful tool in assessing alignment during rTKA. Determining prosthetic position during revision can be difficult and time-consuming, due to major bone loss and the ensuing disappearance of anatomical landmarks. Reduced operation time in the CAS group can

be explained by the fact that CAS makes it easier to determine prosthetic position, outweighing the extra time needed for tracker placement and registration of data points.

This study has some limitations. We were not able to bring in enough patients during the inclusion period as calculated in the power analysis. We decided not to include patients operated before 2002, because at that time a different type of prosthesis was used. We also decided that alignment measurements performed now on patients operated before 2002 were not representative. For this reason, it was not possible to include more patients in the historical control group, and patients that undergo rTKA nowadays will be operated using CAS. Inclusion of patients in the intervention group did not reach the desired number as calculated in the power analysis either. Patients were included until January 2015, so that the results of this study could be presented in this thesis. Given that the literature on CAS-rTKA, especially comparative studies, is limited, and the fact that the influence on rotational alignment has not been described before, this study makes a valuable contribution to the existing literature.

Our study showed no evidence that the use of CAS during revision TKA leads to improved coronal, sagittal or rotational alignment of a knee prosthesis or fewer outliers. Orientation of the tibial component, however, was more internally rotated with the use of CAS, but the proportion in outliers for this measurement in both groups was comparable. The findings of this study must be interpreted with caution, as the number of included patients was low. Future comparative studies with more patients have to be conducted using identical measurement protocols in order to gain better insight into the influence of CAS-rTKA on knee prosthesis alignment.

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Chapter 10

General Discussion

GENERAL DISCUSSION

This thesis is divided into three parts. Objective of the first part was to gain insight into the different options during revision total knee arthroplasty (rTKA). The survival rates between primary and specially designed revision prostheses when implanted during rTKA were compared in **Chapter 2**. **Chapter 3** investigated the mechanical stability of a tibial plateau, implanted with and without a stem when a Trabecular Metal (TM) cone was used to fill up major tibial bone defects.

The second part of this thesis focused on alignment measurements in TKA and the objective was to investigate the application of the EOS system for taking knee prosthesis alignment measurements. To this end, the reliability and validity of EOS when taking EOS 2D and 3D alignment measurements with a knee prosthesis in situ were assessed in **Chapter 4** and **Chapter 5** respectively. With computer-assisted surgery (CAS) it is possible to perform intraoperative alignment measurements to assist in determining optimal prosthetic alignment. This technique is based on 3D modeling, as is the EOS 3D system. In **Chapter 6** pre- and postoperative EOS 3D knee prosthesis alignment measurements were compared with intraoperative imageless CAS knee prosthesis alignment measurements.

The last part of this thesis focused on the role of imageless CAS during TKA (CAS-TKA). The objective was to gain insight into the influence of CAS-TKA on postoperative alignment. The influence of CAS-TKA on postoperative rotational alignment was assessed by conducting a qualitative and systematic review of the literature, which is presented in **Chapter 8**. In **Chapter 7** and **Chapter 9** the influence of CAS during rTKA on postoperative alignment in the coronal, sagittal and rotational planes was investigated by conducting a prospective intervention study with the use of a historical control group.

The present chapter provides an overview and discussion regarding the main findings of the research presented in this thesis for each of the three parts.

PART 1: OPTIONS IN KNEE REVISION SURGERY

Objective of the first part was to gain insight into the different options during revision total knee arthroplasty. Results of **Chapter 2** showed that primary knee prostheses have a significantly worse survival rate than revision prostheses when implanted during rTKA. Results of **Chapter 3** showed that tibial trays without a stem implanted after reconstruction of major bone defects using a TM cone have good mechanical stability.

Revision of a primary total knee prosthesis is a complicated procedure, often due to extensive ligament and bone damage.[1,2] Generally speaking, during primary TKA the collateral ligaments and posterior cruciate ligament are of good quality and a prosthesis without much constraint can be implanted.[3,4] Due to severe ligament and bone damage, a prosthesis with more constraint tends to be necessary during rTKA.[3-5] The use of more constraint also has its downsides. When more constraint is added, the stresses on the bone-cement interface rise and can lead to earlier aseptic loosening.[6] Shortening of prosthetic survival, especially after rTKA, is something that needs to be avoided: rTKA is associated with worse outcome and shorter survival compared to primary TKA,[7,8] and it is not always possible to re-revise after rTKA so arthrodesis or amputation may then be the only available surgical treatment options.[9,10]

As with ligament damage, the degree of bone loss can also account for difficult decisions during rTKA. Major bone deficiencies are seen often and several options exist to fill these defects. The purpose of counteracting bone defects is to create a stable basis on which a knee prosthesis can be implanted. One can choose to fill minor bone defects with bone cement, allograft or autograft material. Major bone defects are generally handled by the implantation of metal augments or even Trabecular Metal (TM) cones.[11] Generally, to accurately implant metal augments additional bone has to be removed to create a stable basis for the augment. Removal of bone can be a difficult decision, as one wants to preserve as much bone as possible, especially in a situation of major bone loss. On the other hand, a stable basis for a knee prosthesis needs to be created and thus metal augments can

be necessary to accomplish that. It comes down to the experience of the orthopedic surgeon to assess the degree of bone damage and to decide how to handle this during rTKA. Another option to be considered during rTKA is the implantation of intramedullary stems. Advantages of using stem extensions in TKA are load-sharing and increased stability by reducing micro-motion, which is especially interesting when a prosthesis with more constraint and/or augments is implanted.[12] Disadvantages include stress-shielding with associated reduction in bone density, risk of subsidence and loosening, periprosthetic fracture and end-of-stem pain.[12]

Primary versus revision knee prostheses

In rTKA a choice can be made to implant a prosthesis that is generally implanted during primary TKA. However, there are specially designed knee prostheses with higher constraint and the option of using augments and stem extensions to counteract for the bone and ligament damage that is frequently seen during rTKA. Downsides of these revision prostheses are that more constraint may theoretically lead to earlier aseptic loosening, and that when augments are placed extra bone has to be removed. Also, stem extensions might give extra stability but may also have negative side effects like stress-shielding. Revision prostheses are also much more costly than primary prostheses. Results of **Chapter 2** of this thesis showed that primary knee prostheses have a significantly worse survival rate than revision prostheses when implanted during rTKA.

A high number of patients is generally included in survival analyses. In this thesis only 69 patients were included, nine of whom received a primary prosthesis and 60 a revision prosthesis. It was decided to only include patients from our own institution. Since the number of annually performed rTKAs is much smaller than primary TKA it was not possible to include more patients in an 11-year time span. Although the number of patients was low, the difference in survival was still outspoken and significant. Survival after five years of the primary prosthesis was 44% compared to 92% for revision prostheses. To gain more insight into the long-term survival and factors

that influence outcome after rTKA, future studies with larger series are necessary.

Choosing degree of constraint, handling bone defects and deciding whether to implant intramedullary stems are all case-specific and come down to the experience and vision of the orthopedic surgeon. For those three major decisions, the benefits have to be balanced against the disadvantages. These decisions may be difficult, especially when no conclusive guidelines are available and most of the decisions depend on the judgment made by the orthopedic surgeon during the surgery. Hence the aim of the first part of this thesis was to provide evidence in order to guide in these decisions. Results of **Chapter 2** indicated that it is questionable whether primary implants are even an option during rTKA, given that the difference in prosthetic survival is so outspoken. Choosing the right type of implant during rTKA is a challenging task. One should beware of underestimating ligament and bone damage and of the risks involved when implanting a prosthesis without sufficient constraint or stability of the construction on which the knee prosthesis is implanted. In the near future it will be interesting to use the data of the Dutch Orthopedic Registry (LROI), which has been collecting input since 2007. For now, when planning a rTKA, one should be prepared to have an availability of revision prostheses during surgery.

Tibial Trabecular Metal cones

When a major bone defect is present, it can be reconstructed by using a TM cone, although it is unknown whether there is a need to implant a tibial base plate with a stem extension onto such a construction. It was hypothesized that when a large tibial bone defect is reconstructed using a TM cone, a stable basis for the tibial component is generated. Additional stability using a stem might not be necessary and the negative side effects of using stem extensions might be avoided. Results of **Chapter 3** showed that tibial components without a stem implanted after reconstruction of a large bone defect with a TM cone have good mechanical stability. Additional

load-sharing and increasing stability using a stem to the tibial base plate in this case is not necessary, so disadvantages of using stem extensions can be avoided.

The study design used in **Chapter 3** was a biomechanical *in vitro* study using cadaveric bone. The forces and number of cycles applied were a simplification of the situation *in vivo*. The aim was to investigate mechanical stability of the proximal tibia after bone defect repair with a tibial TM cone, for which this setup is suitable. To gain more insight into the long-term results of implanting a tibial base plate without a stem extension after reconstruction with a TM cone, *in vivo* studies of larger series have to be conducted.

The various decisions that have to be made during rTKA can be challenging, as no conclusive guidelines are available and decisions are dependent on the judgments made by the orthopedic surgeon. The results presented in **Chapter 3** put into question whether one should implant a tibial base plate with a stem extension should be implanted when a major bone defect is reconstructed using a TM cone.

PART 2: ALIGNMENT MEASUREMENTS IN TKA

The second part of this thesis focused on alignment measurements in TKA. The objective was to investigate the application of the EOS system for taking knee prosthesis alignment measurements. The results of **Chapter 4** showed excellent intra- and interobserver reliability for varus/valgus measurements of the knee joint in 2D (VV2D) as well as 3D (VV3D). There was however a significant difference between the 2D and 3D measurements. The results of **Chapter 5** showed that EOS VV3D measurements of the knee joint are more valid than VV2D measurements. In **Chapter 6** pre- and postoperative EOS 3D knee prosthesis alignment measurements were compared with intraoperative CAS knee prosthesis alignment measurements, showing differences in almost all cases. The EOS 3D measurements overestimated the varus/valgus angle in the lower limbs with a substantial mechanical axis deviation. Also, a systematic bias was present.

Obtaining optimal knee prosthesis alignment during TKA is essential, as malalignment leads to earlier aseptic loosening and revision surgery.[13] Preoperative alignment measurements are important in primary as well as revision TKA for purposes of preoperative planning. Postoperative alignment measurements serve as feedback to the orthopedic surgeon. Moreover, when a patient is not functioning well after TKA, alignment measurements should be taken in order to evaluate whether malfunctioning might be caused by malalignment of the knee prosthesis. Among the options for taking these alignment measurements, long-leg standing radiographs (LLRs) are generally used in clinical practice. These 2D measurements have serious pitfalls though, the most important being that their validity is easily hampered by the position of the patient's lower limb during acquisition. Varus or valgus angle as well as rotation and flexion of the lower limb are shown to influence alignment measurements.[14-17] Previous research has shown a range of up to 28˚ for VV2D measurements taken when flexion and rotation of the lower limb were altered.[15]

EOS

3D measurements were developed to overcome measurement errors due to lower-limb malpositioning. With the EOS stereoradiography system it is possible to take low-dose weight bearing 2D and 3D measurements.[18,19] With this technique, orthogonally coronal and sagittal LLRs are made on which 2D measurements can be taken. Specialized software allows taking 3D measurements by combining these two LLRs. The software was originally designed for lower limbs not containing a knee prosthesis. To meet our needs, we developed an adjusted measurement protocol for this technique to take 3D measurements after TKA and during preoperative planning of rTKA. In **Chapter 4** the intra- and interobserver reliability of the EOS VV2D and VV3D measurements using this measurement protocol were investigated. Both measurements appeared to be excellent, yet significant differences between the two measurements on the same patient were observed. It was hypothesized that the EOS VV3D measurements were valid, while the

EOS VV2D measurements lacked validity as a result of malpositioning. To this end, a validity study using an artificial leg was conducted (**Chapter 5**). In this study varus/valgus angle as well as flexion and rotation of the artificial lower limb were varied. The results showed that altering one of the three position variables did not result in major differences in either VV2D or VV3D. For a combination of the three position variables, however, it was demonstrated that VV3D indeed remained relatively constant while VV2D showed impressive variation. The maximum variety in EOS VV2D measurements found in this study with the same setup when altering the degree of rotation was 16.5˚. The largest differences between the preset varus/valgus angle and the VV2D measurements were found when the leg was in extreme positions, for example 15˚ valgus, 20˚ flexion and 20˚ internal rotation.

Taking measurements using the EOS system also has some limitations, first and foremost in terms of its availability. Our hospital is currently the only institution in the Netherlands to have an EOS system. This technique is also used elsewhere in Europe, Asia and the U.S. The device is relatively new and it is not realistic to expect it to be available on a large scale immediately. The system was originally designed for the follow-up of scoliosis patients[20] and can be used for other types of measurements too, including vertebrae,[21] sagittal balance and spine curves,[22,23] shoulder bony landmarks,[24] pelvic and acetabular morphology,[25] pelvic tilt and acetabular cup orientation,[26] offset and anteversion measurements with and without hip prosthesis,[27] and foot and ankle[28] and lower-limb measurements in children[29] and adolescents.[30] The clinical applications of this new system are expanding rapidly and should be given some time to build a reputation. Secondly, cost-effectiveness of the system is a matter of debate. At present it is stated that the EOS system is less cost-effective compared to conventional LLRs.[31,32] It should be noted however that the cost-effectiveness-calculation of McKenna et al.[32] is based on the financial investment on the EOS system and the potential health benefit of a reduced risk of cancer due to lower radiation exposure. Other advantages, such as the benefits of using EOS to obtain more valid knee prosthesis alignment

measurements and therefore potentially improved outcome after TKA, are not taken into account. An analysis by Dietrich et al.[31] considered not only financial investment and radiation dose but also workflow, patient comfort and financial break-even of LLRs and the EOS system. They concluded that the EOS system, compared to conventional X-ray, reduces radiation exposure, increases subjective noise exposure to patients and demands a higher number of examinations per year for the financial break-even point, despite lower labor costs per examination due to shorter examination time. Since the EOS system is a new technique whose clinical applications and evidence regarding various potential health benefits are still under investigation, the conclusions about cost-effectiveness should be interpreted with caution. The EOS system cannot replace a standard digital radiography system.[31] Thirdly, performing EOS 3D reconstructions take more time than taking measurements on 2D LLRs. Using the EOS system, one can choose between the 'full 3D' and the 'lower-limb alignment' mode. With the full 3D mode an extensive 3D reconstruction is performed and several alignment measurements are taken. With the lower-limb alignment mode fewer alignment measurements are calculated, but 3D reconstructions take less time. Moreover, 3D reconstructions of lower limbs containing a knee prosthesis can only be performed using the lower-limb alignment mode due to the disappearance of anatomical landmarks essential for the full 3D mode. Guenoun et al.[33] stated that a 3D reconstruction of the lower limb using the full 3D mode took about 5 minutes. Time needed to perform a 3D reconstruction using the lower-limb alignment mode is expected to be even shorter. Although 3D reconstructions may take additional time, alignment measurements have to be taken accurately in light of their importance, and a reconstruction time of around 5 minutes or less does not have a high impact.

Knee prosthesis alignment measurements are of major importance in TKA. Although 2D measurements are known to show great variation due to varus or valgus deformity, or flexion or rotation during acquisition, such measurements are still taken on a daily basis in clinical practice. 3D measurements, for example taken by the EOS system, do not show this

amount of variation and might thus be a good alternative for obtaining reliable and valid measurements. When performing 2D measurements one should be aware of their validity, especially when a patient has a severe varus or valgus deformity, a flexion contracture or the coronal image is not taken with frontal accuracy.

EOS versus CAS

Besides pre- and postoperative alignment measurements it is also possible to take alignment measurements intraoperatively using CAS. Since alignment measurements using EOS or CAS are both based on a 3D technique and use the same landmarks, they should theoretically correlate well. Previous studies have shown differences between alignment measurements taken on LLRs and by using CAS.[34-38] Several explanatory factors have been suggested for these differences: the influence of malpositioning during acquisition of LLRs on alignment measurements, the validity and reliability of alignment measurements on LLRs, influence of the weight bearing position on alignment measurements, and a lack of validity and/or reliability of the CAS measurements. In **Chapter 6** EOS 3D measurements were compared with CAS measurements. It was hypothesized that the differences between the two techniques as shown in previous studies could be based on the variability of 2D measurements, as was also demonstrated in **Chapter 5**. By using EOS 3D reconstructions it is unlikely that potential differences between EOS and CAS alignment measurements are caused by the influence of lower-limb positioning during acquisition or errors in the validity or reliability of the EOS 3D measurements. The results of **Chapter 6** showed that, even though EOS 3D reconstructions were used, there were still significant differences in alignment measurements between the two techniques. The EOS 3D measurements overestimated the varus/valgus angle in lower limbs with substantial mechanical axis deviation. Also, a systematic bias between the two measurement techniques was present. These results indicate that the differences are mainly due to the difference between weight bearing and non-weight bearing position as well as a

potential lack of reliability and/or validity of the CAS system.

The use of CAS during TKA is intended to achieve better prosthetic alignment in order to enhance functional outcome and survival rates. Studies on the reliability and validity of this technique are scarce though.[39-41] Besides the effect of the weight bearing position, the results of **Chapter 6** of this thesis may be explained by a lack of reliability and/or validity of the CAS system. Future research on reliability and validity of CAS systems is therefore necessary to gain further insight. Orthopedic surgeons should be aware of this limited evidence and keep it in mind when interpreting CAS measurements.

PART 3: COMPUTER-ASSISTED SURGERY IN TKA

The objective of the last part of this thesis was to gain insight into the influence of CAS during TKA on postoperative alignment. The results of **Chapter 8** showed no evidence that CAS-TKA leads to better rotational alignment. The results of **Chapter 9** showed no evidence that CAS-rTKA leads to improved coronal, sagittal or rotational alignment of a knee prosthesis.

The influence of CAS on rotational alignment

It is known that CAS-TKA improves coronal and sagittal knee prosthesis alignment with fewer outliers than a conventional technique.[42-47] The influence of CAS on rotational alignment and the influence of the technique on postoperative alignment when used during revision surgery are controversial. Malrotation is a known reason for pain after TKA.[48] Besides pain, CAS can also cause problems with patellar tracking, patellar tilt, instability, stiffness and a compromised range of motion.[48-54] A prospective study by Hofmann et al.[53] evaluated 26 patients with pain after TKA; 96% (n=25) had clinically relevant internal rotation of the tibial and/or femoral component, and combined malrotation was found in 38% (n=10) of the cases. Incavo et al.[54] evaluated the outcome after rTKA indicated

for malrotation, and although functional and clinical improvement was observed the results are inferior to those for primary TKA. This stresses the need for proper component rotation during TKA in order to achieve optimal rotational alignment.

Since the introduction of computer navigation there has been a focus on the influence of CAS on coronal and sagittal alignment. Recent studies have evaluated the effect on rotational alignment as well. Gold standard for measuring femoral rotational alignment is to measure the angle between the transepicondylar axis (TEA) and the posterior condylar line (PCL). When determining correct femoral rotation during TKA, several landmarks have to be marked in order for the CAS system to calculate the PCL, TEA and Whiteside line. Van der Linden et al.[55] found a systematic error of 3˚ in determining the TEA with CAS, and his proposed reason was the difficulty in palpating and thus marking the medial and lateral epicondyles during surgery. Two other studies on the potential errors of marking the landmarks found errors of up to 9.1˚ for marking the medial femoral epicondyle and 7.2˚ for marking the lateral femoral epicondyle,[40] and a maximum interobserver error of 8.2˚ in marking the TEA.[41] It was found that reliability of registration of all the anatomical landmarks was low.[40] Although these results may be related to a specific type of CAS system, the difficulty in registering the landmarks and potential errors in both validity and reliability of CAS measurements is clear. There is no gold standard for measuring tibial rotational alignment. References used for measurements include the tip and medial third of the tuberosity,[47,50,56] ankle[57] and posterior border of the proximal tibia.[58]

We conducted a systematic review on the influence of CAS during TKA on postoperative rotational alignment (**Chapter 8**). This review showed no evidence that use of CAS during TKA improves rotational alignment or reduces the number of rotational outliers. This conclusion should be interpreted with caution though. The number of studies included was low (n=17), as CAS is a relatively new technique and its effect on rotational

alignment has not been widely investigated yet. Only one of the included studies was considered of high methodological quality, and in only one study was the sample size calculation based on one of the outcome measures used in this review. Almost all of the studies are thus potentially underpowered. There is no gold standard for assessing rotational alignment of the tibial component, which makes study results difficult to compare. To gain more insight into the effect of CAS-TKA on rotational alignment, more studies of high methodological quality with sample size calculations based on one of the outcome measures have to be conducted. The outcome measures, especially rotation of the tibial component, should be obtained using the same measurement protocol.

Limited evidence on the reliability and validity of CAS systems exists and may also be system-specific. Future research on specific CAS systems should therefore be conducted in order to gain insight into potential errors and on whether this is related to particular systems.

Due to the recent introduction of CAS systems, most research has focused on the influence of CAS on postoperative alignment. The limited research on clinical outcome after CAS-TKA is only available for the short- and mid-term and does not show improvement compared to conventional methods.[59,60] Given that alignment is improved and thus survival rates may be improved, it is too early to determine this effect. Studies with larger sample sizes and longer follow-up should provide more insight into the impact of CAS-TKA on clinical and functional outcome and survival rate.

The use of CAS during revision TKA

Little is known about the use of CAS during rTKA. The results of **Chapter 9** showed no evidence that CAS-rTKA leads to improved coronal, sagittal or rotational alignment of a knee prosthesis. Unfortunately, this study did not reach the desired number of included patients and may thus be underpowered. Although the study failed to show improved postoperative alignment after CAS-rTKA in **Chapter 9**, CAS during rTKA appeared to be a very useful tool. Determining prosthetic position during rTKA can be

difficult and time-consuming, due to major bone loss and the ensuing disappearance of anatomical landmarks. Since CAS makes this process easier, we believe this is also the reason why we did not find a prolonged operation time, which was mentioned in several other studies.[59,61] The introduction of CAS has also underlined the importance of prosthetic alignment. This technique forces the orthopedic surgeon to specify what is understood by optimal prosthetic alignment and what the potential consequences of malalignment are. There is evidence that prosthetic alignment using conventional methods has improved after the introduction of CAS.[62] The use of CAS has also reduced the learning curve of joint arthroplasty.[63,64]

To our knowledge, only two other comparative studies on CAS-rTKA[65,66] have been conducted yet, hence the results of this study are a valuable contribution to the limited literature on the topic. More comparative studies on the use of CAS-rTKA of higher methodological quality should be conducted to gain insight into the influence of CAS-rTKA on postoperative alignment and clinical and functional outcome.

The use of CAS during TKA and rTKA is a relatively new technique for which conclusive evidence on the reliability and validity of specific systems, long-term outcome and results when used in rTKA is lacking. CAS gives surgeons the ability to provide for constant feedback during TKA, which is of extra importance during rTKA. Orthopedic surgeons should be aware of potential errors of the CAS system used, as well as of the potential benefits this technique provides. Constant feedback, resulting in better notification of cutting errors and consequently correction and improved coronal and sagittal alignment are among the benefits of using CAS. It is therefore advised to rely not solely on CAS measurements but to consider this technique to be a helpful assistive tool in obtaining optimal prosthetic alignment during TKA. Although the technique has disadvantages and much research still has to be conducted, it has generated a focus on the importance of knee prosthesis alignment. Giving attention to this topic by itself is a benefit of introducing this technique.

PUBLIC HEALTH BENEFITS

With the increasing number of patients undergoing primary and revision TKA as a result of end-stage OA, further refinement of the surgical procedure is of eminent importance - especially as the proportion of younger patients still active in the workforce is rising. The innovative techniques described in this thesis can be helpful toward improving prosthetic survival, functioning of the patients and – in the end – participation in society.

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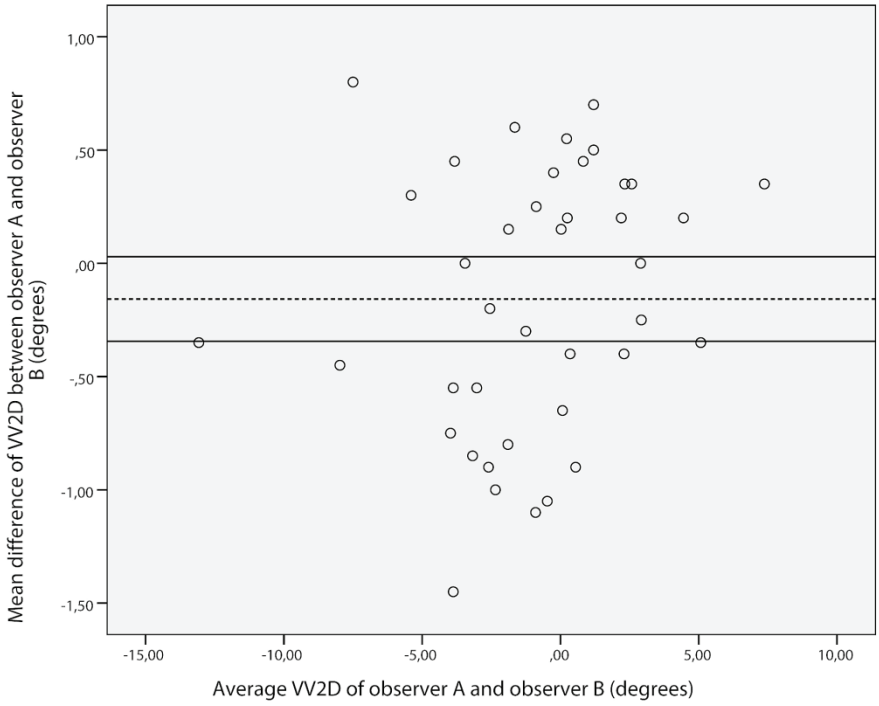
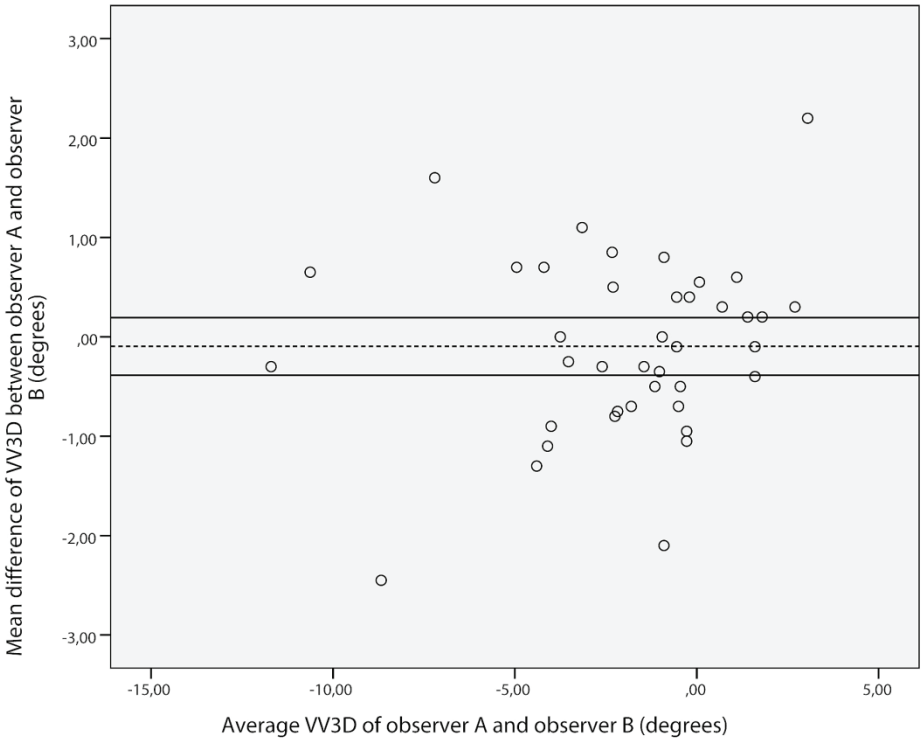
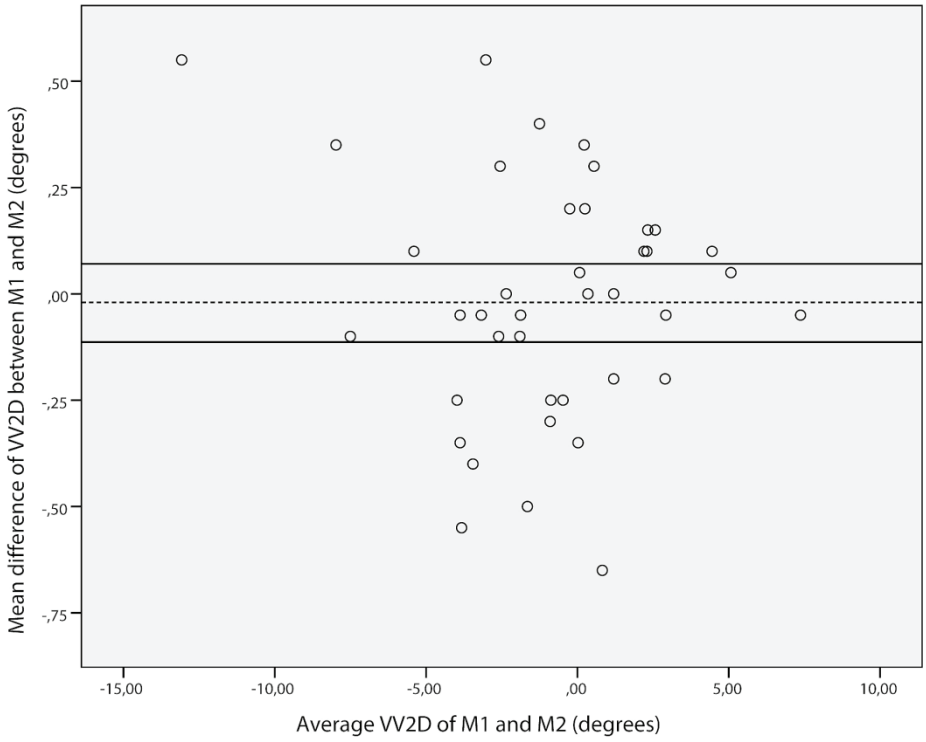
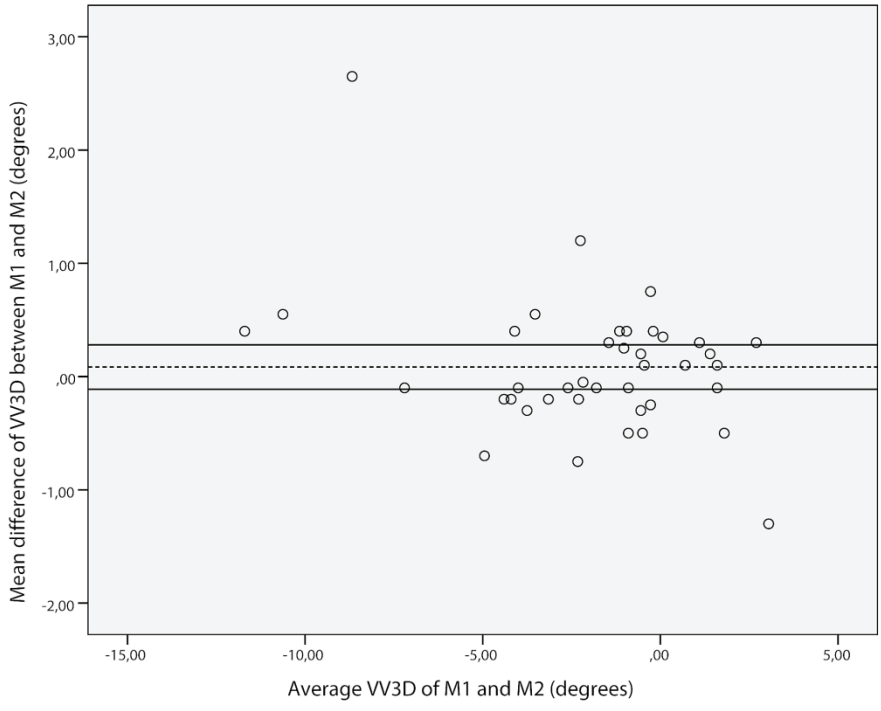
Appendix

CHAPTER 4: SCATTER PLOTS OF THE BLAND & ALTMAN METHOD






Mean difference of VV2D between M1 and M2 (degrees)
,50
,25
,00
-,25
-,50
-,75
-15,00
-10,00
-5,00
,00
5,00
10,00
Average VV2D of M1 and M2 (degrees)


Mean difference of VV3D between M1 and M2 (degrees)
3,00
2,00
1,00
,00
-1,00
-2,00
-15,00
-10,00
-5,00
,00
5,00
Average VV3D of M1 and M2 (degrees)

CHAPTER 4: TABLES OF THE DISTRIBUTION OF OUTLIERS

Outlier distribution of intraobserver reliability for VV2D

		VV2D M2		Total
		No outlier	Outlier	
VV2D M1	No outlier	26	1	27
	Outlier	0	13	13
Total		26	14	40

Outlier distribution of intraobserver reliability for VV3D

		VV3D M2		Total
		No outlier	Outlier	
VV3D M1	No outlier	27	1	28
	Outlier	0	12	12
Total		27	13	40

Outlier distribution of interobserver reliability for VV2D

		VV2D Observer B		Total
		No outlier	Outlier	
VV2D Observer A	No outlier	24	1	25
	Outlier	3	12	15
Total		27	13	40

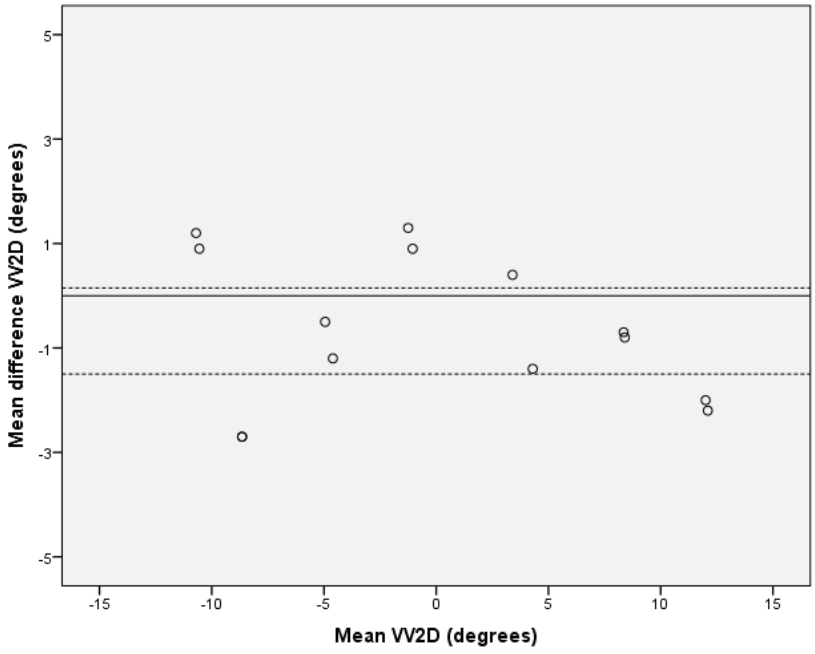
Outlier distribution of interobserver reliability for VV3D

		VV3D Observer B		Total
		No outlier	Outlier	
VV3D Observer A	No outlier	27	1	28
	Outlier	1	11	12
Total		28	12	40

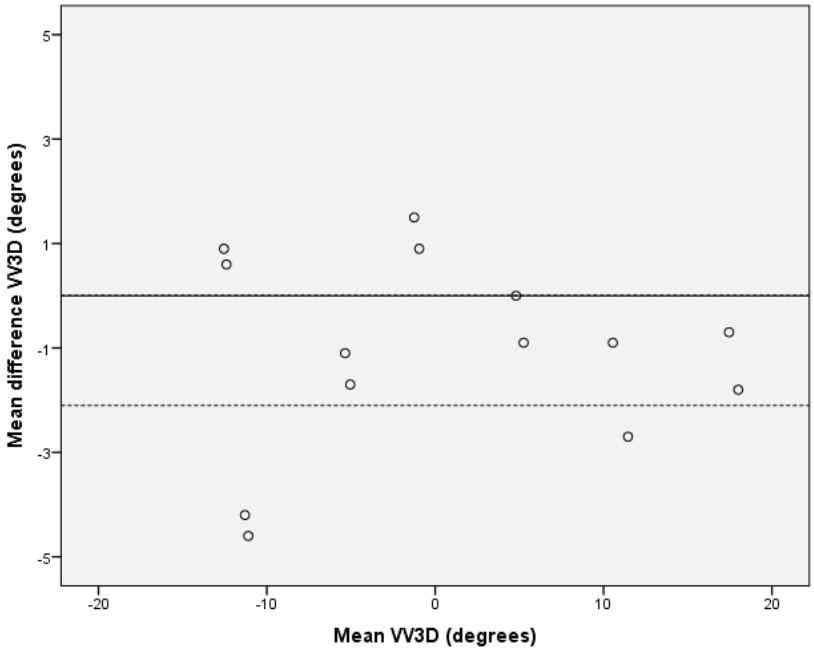
Outlier distribution of VV2D versus VV3D

		VV2D		Total
		No outlier	Outlier	
VV3D	No outlier	22	5	27
	Outlier	4	9	13
Total		26	14	40

CHAPTER 5: ABSOLUTE INTRAOBSERVER RELIABILITY



Absolute intraobserver reliability did not show a systematic bias for VV2D.



Absolute intraobserver reliability did not show a systematic bias for VV3D.

CHAPTER 5: THE INFLUENCE OF ROTATION, FLEXION AND VARUS/VALGUS ANGLE ON EOS 2D AND 3D VARUS/VALGUS MEASUREMENTS

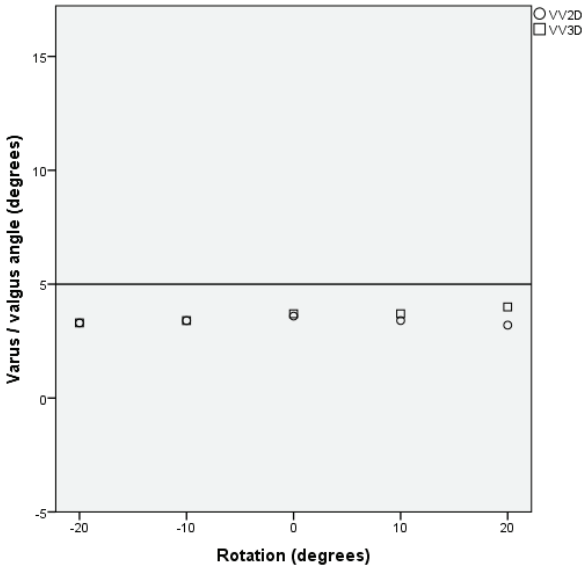


Fig 1. The preset varus/valgus was 5˚ valgus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

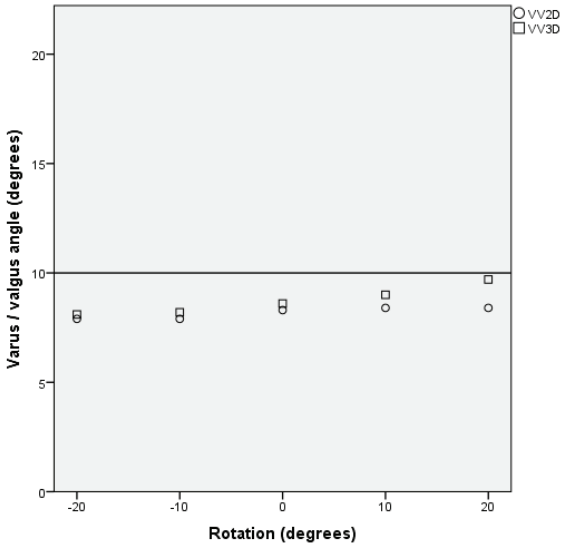


Fig 2. The preset varus/valgus was 10˚ valgus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

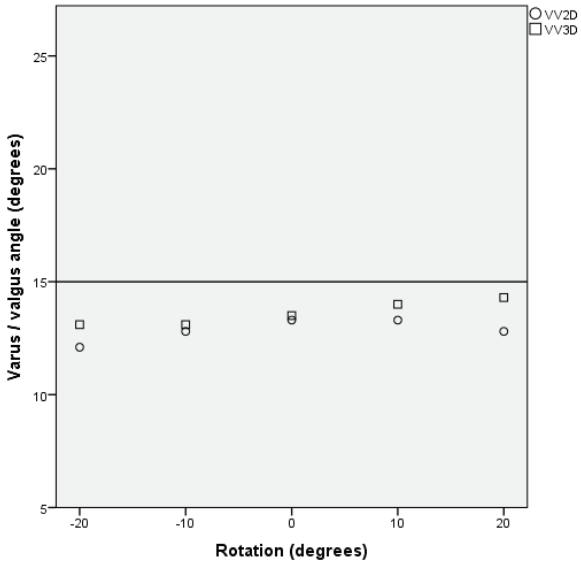


Fig 3. The preset varus/valgus was 15˚ valgus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

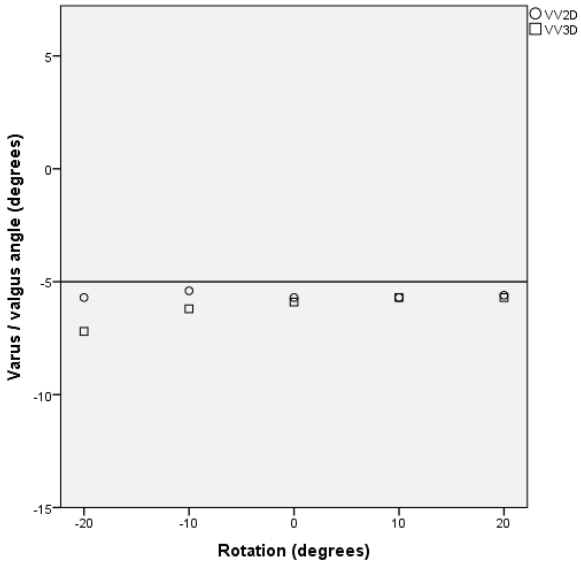


Fig 4. The preset varus/valgus was 5˚ varus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

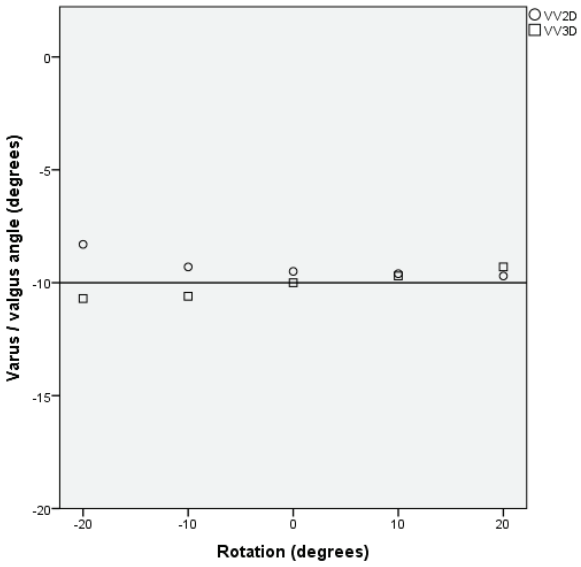


Fig 5. The preset varus/valgus was 10˚ varus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

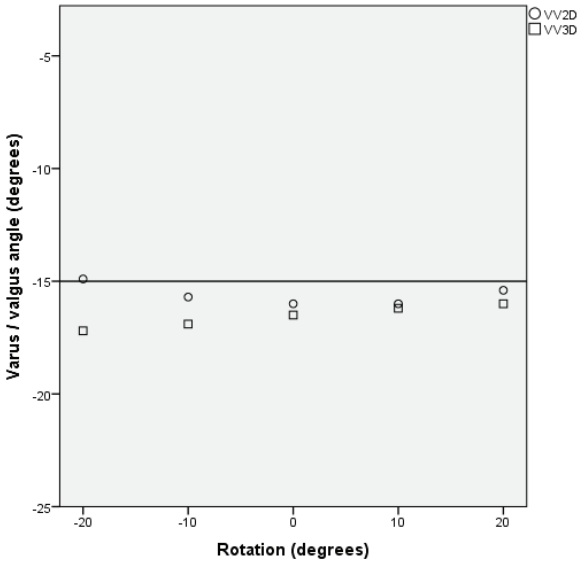


Fig 6. The preset varus/valgus was 15˚ varus, flexion angle was 0˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

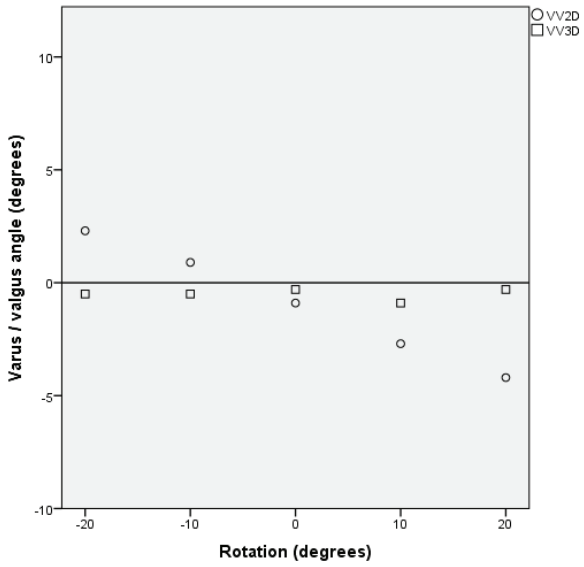


Fig 7. The preset varus/valgus was 0˚, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

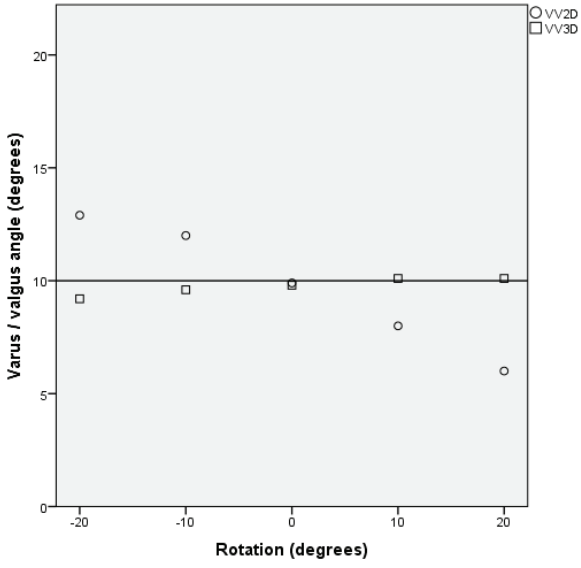


Fig 8. The preset varus/valgus was 10˚ valgus, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

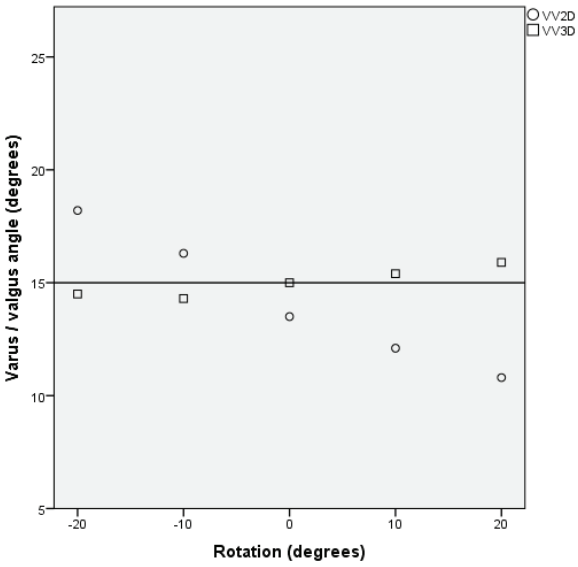


Fig 9. The preset varus/valgus was 15˚ valgus, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

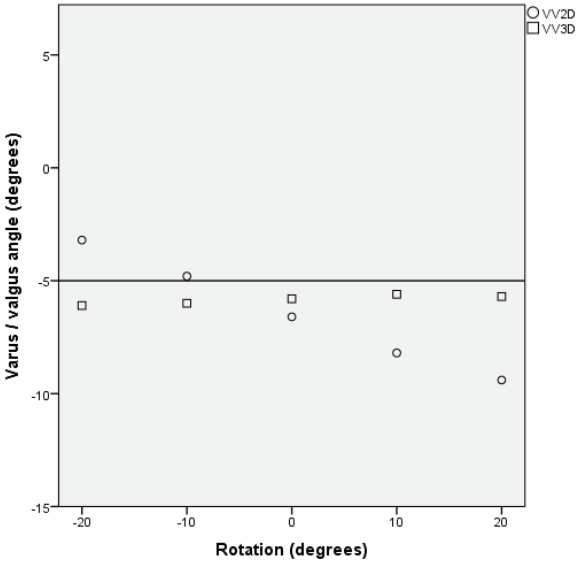


Fig 10. The preset varus/valgus was 5˚ varus, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

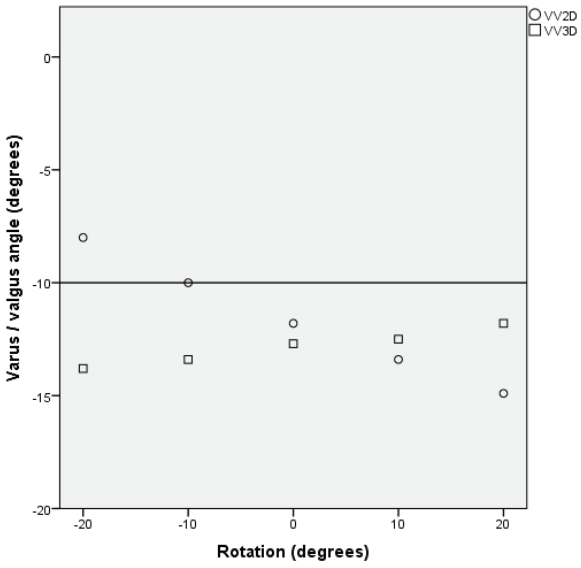


Fig 11. The preset varus/valgus was 10˚ varus, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

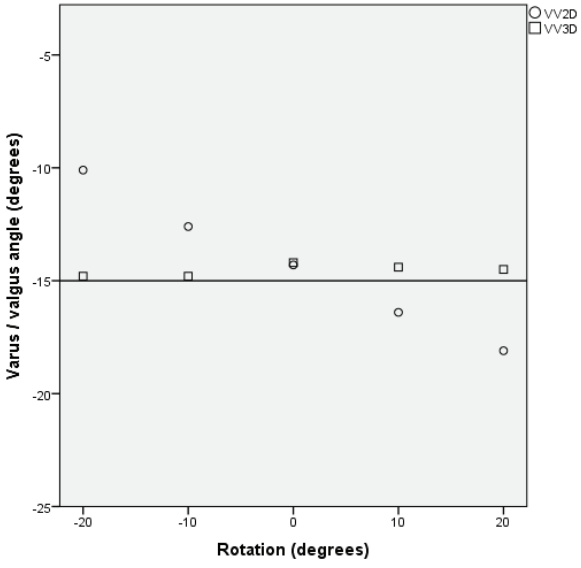


Fig 12. The preset varus/valgus was 15˚ varus, flexion angle was 10˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

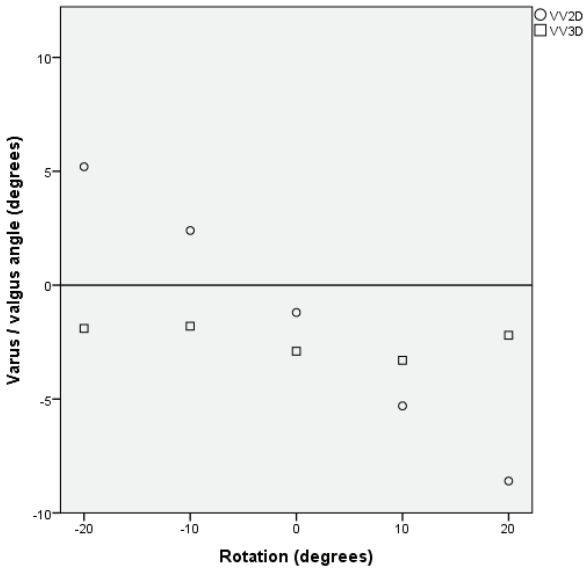


Fig 13. The preset varus/valgus was 0˚, flexion angle was 20˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

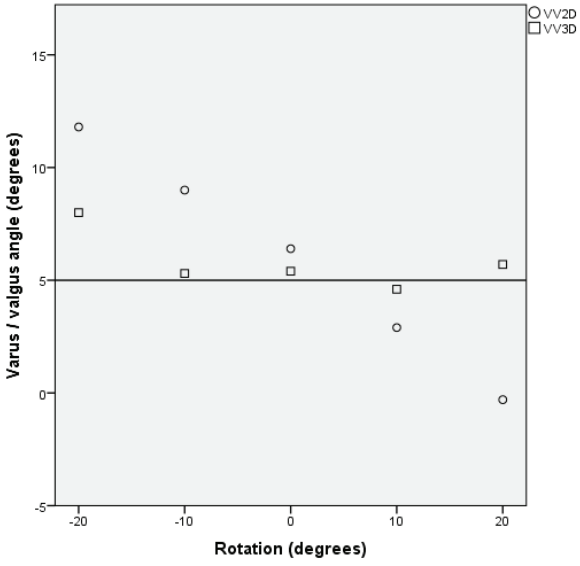


Fig 14. The preset varus/valgus was 5˚ valgus, flexion angle was 20˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

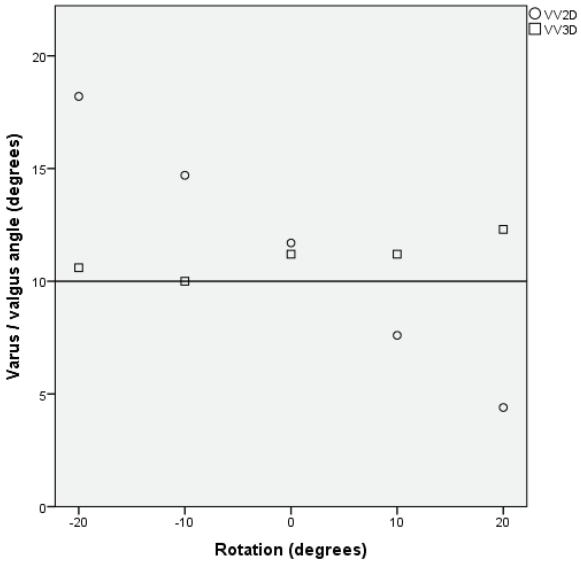


Fig 15. The preset varus/valgus was 10˚ valgus, flexion angle was 20˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

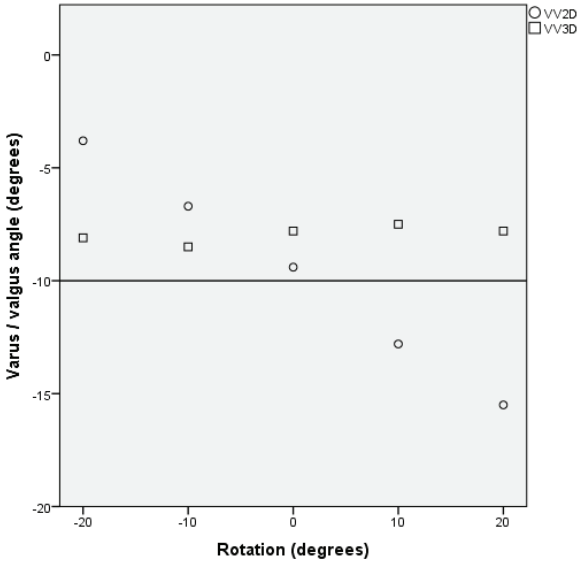


Fig 16. The preset varus/valgus was 10˚ varus, flexion angle was 20˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

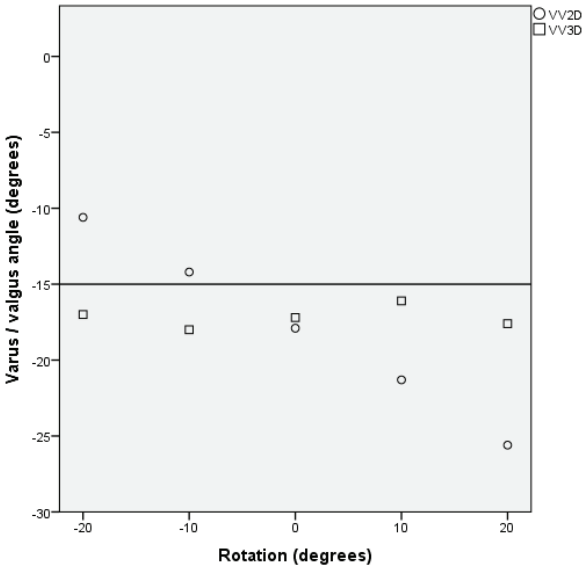


Fig 17. The preset varus/valgus was 15˚ varus, flexion angle was 20˚ and rotation was varied from 20˚ internal rotation to 20˚ external rotation with 5˚ increments.

CHAPTER 8: STUDY CHARACTERISTICS

Study	Number	Method	Participants	Navigation system
Blakeney et al.[18]	66	RCT	Patients undergoing TKA to treat knee osteoarthritis and varus deformity. Exclusion criteria: valgus deformity or tibial deformity from previous fracture and/or osteotomy.	BrainLab Knee essential software (BrainLab, Feldkirchen, Germany) for the Genesis-II system
Carter et al.[43]	200	CCT	Intervention group consisted of all primary TKAs from the fall of 2003 until 100 TKAs were included. Conventional patients were recruited in reverse sequence from the date of navigation adoption.	Stryker Knee Navigation system (Stryker Instruments, Kalamazoo, MI, USA)
Chauhan et al.[41]	12	Cadaveric study	Cadaveric study performed on six cadavers that were treated with "soft-fix" fixative.	Stryker Knee Navigation system (Stryker Instruments, Kalamazoo, MI, USA)
Chauhan et al.[38]	75	RCT	Patients awaiting TKA. Matched for age, height, weight, BMI, ASA grade, and preoperative deformity of the limb. Exclusion criteria: active infection, malignancy.	Stryker Knee Navigation system (Stryker Instruments, Kalamazoo, MI, USA)
Choong et al.[14]	104	RCT	Patients scheduled for primary TKA between June 2005 and July 2006.	Ci System, DePuy (DePuy Orthopaedics, Inc., Warsaw, IN, USA)

Measured rotational alignment	Reported outliers	Additional information
Femoral rotation and tibiofemoral mismatch	Femoral rotation	All surgeries were performed by one experienced knee arthroplasty surgeon who was familiar with all techniques.
Femoral and tibial rotation (according to the protocol of Berger et al.[10])	Femoral and tibial rotation (according to the protocol of Berger et al.[10])	Surgeries were performed by three surgeons. On the evening before the first 4 navigated surgeries, the three surgeons and surgical personnel went through a sawbones demonstration as the only special training before start of this study.
Not reported	Femoral rotation and tibiofemoral mismatch	Two surgeons performed the surgeries. Both had some experience in conventional TKA but were relatively new to CAS.
Not reported	Femoral and tibial rotation (according to the Perth CT protocol as described by Chauhan et al.[41]) and tibiofemoral mismatch	All surgeries were performed by one surgeon who had performed more than 250 conventional TKAs and 12 CAS TKAs before this trial.
Femoral rotation	-	All surgeries were performed by 3 senior arthroplasty surgeons who had a minimum of 18' months experience each with conventional and CAS TKAs before commencement of this trial. All surgeons attended a 2-day learning center focusing on the instruments, software, and technique of CAS before using the CAS systems in the institution.

Study	Number	Method	Participants	Navigation system
Han et al.[42]	55	RCT	Patients undergoing primary TKA between July and December 2005 for treatment of knee osteoarthritis. Exclusion criteria: history of tibial or femoral fractures or pyogenic arthritis of knees in a growth period.	OrthoPilot navigation system (B. Braun Aesculap, Tuttlingen, Germany)
Hiscox et al.[29]	32	RCT	Patients older than 18 years undergoing primary TKA between May 2004 and July 2005 for treatment of knee arthritis. Subgroup analysis of first 15 patients of each arm. Exclusion criteria: deformity of the femur preventing use of an intramedullary guide and deformity or instability that necessitated use of knee implants with intramedullary stems.	Stryker Knee Navigation system (Stryker Instruments, Kalamazoo, MI, USA)
Kim et al.[44]	320	RCT	Patients with osteoarthritis undergoing primary bilateral TKAs between January 2003 and March 2004. One knee was replaced using CAS and the other conventionally.	Vector Vision CT-free knee (BrainLab, Munich, Germany)
Kim et al.[39]	200	RCT	Patients undergoing bilateral primary TKAs for osteoarthritis. One knee was replaced using CAS and the other conventionally. Exclusion criteria: varus deformity greater than 20° or valgus deformity greater than 30°.	Vector Vision CT-free knee (BrainLab, Munich, Germany)
Lützner et al.[37]	80	RCT	The patients included had primary or secondary osteoarthritis of the knee, no previous hemi- or total arthroplasty, a mechanical axis between 20° varus and 5° valgus, and no severe instability that could not be treated with an unconstrained, cruciate-retaining prosthesis.	Stryker Navigation System, Knee Navigation Software V3.1 (Stryker Instruments, Kalamazoo, MI, USA)

Measured rotational alignment	Reported outliers	Additional information
Femoral rotation	Femoral rotation	All surgeries were performed by one surgeon.
Femoral and tibial rotation (according to the protocol of Berger et al.[10]) and tibiofemoral mismatch	-	The study was completed at an academic arthroplasty center by three fellowship-trained arthroplasty surgeons who each performed greater than 100 TKAs per year. Each surgeon had performed between 5 and 20 CAS TKAs before study initiation.
Femoral and tibial rotation (as described by Matziolis et al.[9])	Femoral and tibial rotation (as described by Matziolis et al.[9])	All surgeries were performed by one surgeon.
Femoral and tibial rotation (tibial component relative to the posterior margin of proximal tibia)	Femoral and tibial rotation (tibial component relative to the posterior margin of proximal tibia)	All surgeries were performed by one surgeon.
Femoral and tibial rotation (as described by Matziolis et al.[9])	Femoral and tibial rotation (as described by Matziolis et al.[9])	All the patients were operated on by two surgeons trained in navigated TKA.

Study	Number	Method	Participants	Navigation system
Matos et al.[30]	42	RCT	Patients older than 55 years with advanced degenerative knee disease, Ahlbäck 4 or 5, without previous TKA. Exclusion criteria: severe instability of knee with indication of constrained prosthesis.	TKA 4.0 software of the Orthopilot navigation system (Aesculap Orthopaedics, Tuttlingen, Germany)
Matziolis et al.[9]	60	RCT	Patients with presence of primary arthritis of the knee. Exclusion criteria: patients who had previous surgery on the joint or who could not be treated with an unconstrained TKA with a short stem.	PiGalileo System (Plus Orthopedics AG, Rotkreuz, Switzerland)
Mombert et al.[40]	42	RCT	Primary TKA.	Vector Vision TKR Navigation system (BrainLab AG, Heimstetten, Germany)
Schmitt et al.[31]	47	RCT	Patients older than 50 years with primary gonarthrosis and willing and able to give informed consent. Exclusion criteria: patients with rheumatoid arthritis, history of local infections, and gonarthrosis secondary to trauma.	KneeTrac (Stryker Howmedica Osteonics, Mahwah, NJ, USA)
Stöckl et al.[45]	64	RCT	Patients older than 18 years with osteoarthritis, avascular necrosis, or not severe posttraumatic arthritis requiring primary TKA. No previous osteosynthesis of the knee during last 12 months. Exclusion criteria: active infection, malignancy, neurologic deficit, concurrent illnesses that are likely to affect their outcome.	Stryker Knee Navigation System (Stryker Leibinger, Software Vs 1.01) (Stryker Instruments, Kalamazoo, MI, USA)

Measured rotational alignment	Reported outliers	Additional information
Not reported	Femoral rotation	All surgeries were performed by the same surgeon, a specialist in knee replacements and experienced in the navigated technique.
Femoral and tibial rotation (as described by Matziolis et al.[9])	Femoral rotation (as described by Matziolis et al.[9])	-
Femoral rotation	-	-
Tibial rotation (tibial component relative to the ankle)	Tibial rotation (tibial component relative to the ankle)	All surgeries were performed by two surgeons.
Femoral rotation and tibiofemoral mismatch	-	Six surgeons participated in the study.

Study	Number	Method	Participants	Navigation system
Zhang et al.[19]	64	RCT	Bilateral TKAs between March 2007 and June 2008 with one knee treated with conventional TKA and the other with CAS TKA and both knees suitable for placement of a posterior cruciate-retaining prosthesis. All had bilateral osteoarthritis.	Vector Vision CT-free navigation system (BrainLab, Feldkirchen, Germany)
Zhang et al.[32]	81	RCT	Patients with osteoarthritis treated with primary TKA between January 2006 and March 2007. Exclusion criteria: prior deformity correction/osteotomy, greater than 15° varus/valgus deformity, severe osteoporosis, local or systemic signs of acute infection, patients with malignancy.	Stryker Knee Navigation System (Stryker-Navigation, Kalamazoo, MI, USA)

CT = randomized controlled trial; CCT = controlled clinical trial; ASA = American Society of Anesthesiologists; CAS = computer-aided surgery.

Measured rotational alignment	Reported outliers	Additional information
Femoral rotation	-	-
Femoral and tibial rotation (according to the protocol of Berger et al.[10]) and tibiofemoral mismatch	Femoral and tibial rotation (according to the protocol of Berger et al.[10])	All surgeries were performed by one surgeon.

Summary

Osteoarthritis (OA) is the most common joint disorder. Total knee arthroplasty (TKA) is considered to be the gold standard for the surgical treatment of end-stage OA. The incidence of TKA is on the rise and is expected to grow further. Despite good results after primary TKA, a significant proportion of the patients need to have their knee prosthesis replaced, and an increase of the number of these so called revision TKAs (rTKAs) is also seen and is expected to grow further. Besides infection, instability and aseptic loosening of the prosthesis are important reasons for rTKA as well as re-revision TKA. Aseptic loosening can be caused by malalignment of the knee prosthesis. Correct ligamentous balancing and achieving optimal prosthesis alignment during primary and revision TKA are thus essential for obtaining optimal prosthesis survival. By optimizing the surgical technique, the outcome after TKA may be improved and failure of a knee prosthesis may be prevented.

This thesis focuses on new techniques in rTKA and is divided into three parts: the first part focuses on options in knee revision surgery when it comes to (components of) prostheses, the second part on alignment measurements in TKA and the last part on computer-assisted surgery (CAS) in (r)TKA.

The first part of this thesis starts with **Chapter 2**, in which survival rates were compared between primary and specially designed revision prostheses when implanted during rTKA. Results of this study showed that primary implants had a significantly worse survival rate compared to revision implants when implanted during rTKA. After 5 years, 44% of the primary implants were still in situ, compared to 92% of the revision implants. Thus, it was concluded that it is questionable whether implanting a primary implant is even an option during rTKA. In **Chapter 3** a biomechanical study is described. In this study the mechanical stability of a tibial component was assessed when implanted with and without a stem when a Trabecular Metal (TM) cone was used to fill up major bone defects. TM cones are designed to fill up major bone defects in TKA. Tibial components can be implanted in combination with a stem, but it is unclear whether this is necessary after reconstruction with a TM cone. Implanting a stem may give extra stability, but may also have negative side-effects. Tibial revision arthroplasties were performed after reconstruction of major bone defects with TM cones. Plateaus were implanted in seven pairs of cadaveric tibiae; one tibia of each pair was implanted with a stem, the other without. All specimens were loaded to one bodyweight alternating between the medial and lateral tibial plateau. Implant-bone micro motions, bone strains and bone mineral density were compared between the two groups. Results of this study showed that tibial components, with or without a stem, produce very similar biomechanical conditions in terms of stability and strain

distribution and therefore, additional stem extension of the tibial component may not be required.

The second part of this thesis focuses on alignment measurements in TKA. A new low-dose X-ray device, called EOS, has been introduced for determining lower-limb alignment in 2D and 3D. However, reliability and validity of these measurements using this technique when a lower limb contains a knee prosthesis had not been investigated yet. **Chapter 4** describes a reliability study in which intraobserver and interobserver reliability of EOS 2D and 3D varus / valgus (VV) measurements after rTKA were investigated. Results of this study showed that reliability of VV measurements in both 2D and 3D were excellent. However, significant differences existed between 2D and 3D when measured in the same patient. It was hypothesized that this difference could be caused by the influence of lower limb positioning during acquisition on 2D measurements. Measurements in 3D mathematically correct for this potential malpositioning and might thus be more valid. To investigate this further, the influence of flexion, VV angle and rotation of the lower limb on VV measurements in 2D and 3D were investigated using an artificial leg containing a knee prosthesis in **Chapter 5**. Differences between the actual VV position of the artificial leg and its position as measured on EOS 2D and 3D images were investigated. Results of this study showed that the VV measurements in 3D were more valid than in 2D, thus indicating that 3D compensates for malpositioning during acquisition while 2D does not. Therefore, caution is warranted when measuring VV angle on a conventional radiograph of a knee with a flexion contracture, varus or valgus angle and / or rotation of the knee joint during acquisition. **Chapter 6** describes a comparative study of intraoperative alignment measurements using an imageless CAS system with pre- and postoperative EOS 3D alignment measurements. Results of this study show that EOS 3D measurements significantly overestimate VV angle in lower limbs with substantial mechanical axis deviation. For lower limbs with minor mechanical axis deviation, CAS significantly measures more valgus than EOS. The mechanical medial proximal tibial angle is also measured more valgus by CAS. Findings of this study can possibly be explained by the difference between weight bearing and non-weight bearing position and potential errors in validity and reliability of the CAS system. Surgeons should be aware of these measurement differences and the pitfalls of both measurement techniques.

The third part of this thesis focuses on the use of CAS during (r)TKA and starts with **Chapter 7**. This chapter describes the design of a prospective clinical intervention study in which rTKA (CAS-rTKA) is compared with a conventional technique by means

of a historical control group. In primary TKA, CAS leads to better prosthetic alignment than mechanical navigation guides. Literature about CAS-rTKA is scarce though, and the effect on rotational prosthetic alignment has not been investigated yet. Hence the objective of this study was to compare rotational, coronal and sagittal prosthetic alignment after CAS-rTKA compared to a mechanical navigation guide. Results of this study are presented in Chapter 9. **Chapter 8** describes a qualitative and systematic review of the literature on the effectiveness of imageless CAS during TKA (CAS-TKA) on rotational alignment of the femoral and tibial components and tibiofemoral mismatch in terms of deviation from neutral rotation, and the number of femoral and tibial rotational outliers. Seventeen studies were included. Results of this systematic review show no evidence that CAS-TKA leads to better rotational alignment of the femoral or tibial component or tibiofemoral mismatch. Also, no evidence was found that it decreases the number of outliers in terms of femoral or tibial component orientation. However, results of this systematic review have to be interpreted with caution. The number of included studies was low, only one of the 17 included studies was considered of high methodologic quality, and different methods for assessing tibial component rotation were used in the studies. In only one of the included studies the sample size calculation was based on one of the outcome measures. In **Chapter 9** it was investigated whether CAS-rTKA improves coronal, sagittal and rotational knee prosthesis alignment and reduces the amount of outliers compared to a conventional technique. In this prospective clinical intervention study 29 patients (31 knees) were operated using CAS (CAS-rTKA). This group was compared with a historical control group (CON-rTKA), in which 23 patients (23 knees) were operated using the conventional technique. Postoperative alignment was measured using the EOS 2D/3D system (coronal and sagittal planes) and CT-scan (rotation). The results show no evidence that CAS-rTKA leads to improved coronal, sagittal or rotational alignment of a knee prosthesis or less outliers. The tibial component, however, was placed more internally rotated with use of CAS, but the proportion in outliers for this measurement in both groups were comparable. However the findings of this study have to be interpreted with caution, since the number of included patients was low.

The General Discussion in **Chapter 10** provides an overview and discussion of the main findings of the research presented in the previous chapters. Although evidence was found that primary implants have a significantly worse survival compared to revision implants when implanted during rTKA, choosing the degree of constraint, handling of bone defects and whether or not to implant intramedullary stems during TKA are all case-specific and come down to the experience and vision of

the orthopaedic surgeon. Decisions may be difficult, especially when no conclusive guidelines are available and a great proportion of the decisions is dependent on the judgments made by the orthopedic surgeon during rTKA. Survival of primary implants being significantly worse than revision implants, might indicate underestimation of ligament and bone damage which leads to implanting a prosthesis without sufficient constraint or stability. As with the type of prosthesis, how to handle bone defects also comes down to experience and vision of the orthopaedic surgeon. Since stability of a tibial base plate without stem is comparable with one with stem extension after reconstruction of a major bone defect with a TM cone, it is questionable if a stem is necessary.

In this thesis lower limb alignment measurements in 2D as well as 3D are investigated. 2D measurements have some serious pitfalls but are still widely performed though, due to experience and availability in hospitals. It is not expected that 2D will soon be replaced by 3D measurements, since this is a financial investment for hospitals. Moreover, a 3D system does not replace a 2D system. When performing 2D measurements one should be aware of its validity, especially when a patient has a severe varus or valgus deformity, flexion contraction or the coronal image is not taken precisely frontally.

There is no evidence that CAS-TKA improves rotational alignment. However, research about this topic is limited. Moreover, no gold standard for measuring rotation of the tibial component exists yet and therefore results of different studies are not comparable. Besides alignment, there is limited research available that focuses on functional outcome after CAS-TKA and long-term results are not reported. Different systems are used and evidence regarding reliability and validity of CAS systems is scarce and may also be system-specific. No evidence was found that CAS-rTKA improves postoperative alignment. However, the study was underpowered, which might have influenced the results as well. However, the orthopaedic surgeons who performed the CAS-rTKAs experienced the technique as a helpful assistive tool, especially during a complicated surgery as is rTKA. Although the technique has disadvantages and much research still has to be performed, it has generated a focus on the importance of knee prosthesis alignment.

Finally, the General Discussion focuses on public health benefits and states that the innovative techniques described in this thesis can be helpful in improving the survival of the prosthesis, functioning of the patients and – in the end – participation in society.

Samenvatting

Artrose is de meest voorkomende gewrichtsaandoening. Totale knieartroplastiek (TKA) wordt gezien als de gouden standaard als het gaat om de chirurgische behandeling van artrose in een vergevorderd stadium. De incidentie van TKA neemt toe en zal naar verwachting in de toekomst nog verder toenemen. Ondanks goede resultaten na een TKA, heeft een deel van de patiënten een heroperatie, oftewel een revisie TKA (rTKA), nodig. Ook het aantal rTKA's stijgt en de verwachting is dat in de toekomst het aantal verder zal toenemen. Naast infectie (septisch), zijn instabiliteit en aseptische loslating de voornaamste redenen voor rTKA. Aseptische loslating kan veroorzaakt worden door een incorrecte positie (alignement) van de knieprothese. Het verkrijgen van stabiliteit en een correcte prothese-positie tijdens TKA zijn essentieel voor een goed resultaat. Door het optimaliseren van de chirurgische techniek wordt de uitkomst na TKA mogelijk verbeterd en falen van de prothese tegengegaan.

Dit proefschrift gaat over nieuwe technieken op het gebied van rTKA en is onderverdeeld in drie delen: het eerste deel gaat over mogelijkheden op het gebied van protheses en prothese-onderdelen tijdens rTKA, het tweede deel gaat over het meten van prothese alignement en het laatste deel over het gebruik van computernavigatie (CAS) tijdens (r)TKA.

Het eerste deel gaat over mogelijkheden op het gebied van protheses en prothese-onderdelen. Het begint met **Hoofdstuk 2**, waarin de overleving van primaire protheses en speciaal ontwikkelde revisie protheses is vergeleken wanneer deze geïmplanteerd worden tijdens rTKA. De resultaten van deze studie laten zien dat primaire protheses een significant slechtere overleving hebben in vergelijking met revisie protheses. Na vijf jaar was 44% van de patiënten die een primaire prothese had gekregen en 92% van de patiënten die een revisie prothese hadden ontvangen nog niet opnieuw geopereerd. Het is daarom de vraag of het wel verstandig is om een primaire prothese te plaatsen tijdens rTKA. **Hoofdstuk 3** beschrijft een biomechanische studie waarin de mechanische stabiliteit van een tibia component is vergeleken met en zonder steel na reconstructie van een groot botdefect met een Trabecular Metal (TM) cone. TM cones zijn ontwikkeld voor de reconstructie van grote botdefecten tijdens TKA. Na reconstructie kan een tibia component met een steel worden geïmplanteerd, maar het is onbekend of dit noodzakelijk is. Een steel geeft extra stabiliteit, maar heeft ook nadelen. Zeven paar kadaver tibiae waarbij een groot botdefect werd gereconstrueerd met een TM cone werden gebruikt: per paar ontving één tibia een tibia component met een steel en de ander een tibia component zonder steel. Vervolgens werden alle tibiae biomechanisch belast en

werden microbewegingen, rekken en botdichtheid tussen de groepen vergeleken. De resultaten van deze studie laten zien dat tibia componenten met en zonder steel vergelijkbare stabiliteit laten zien na reconstructie van een groot botdefect met een TM cone. Dit suggereert dat het gebruik van een steel mogelijk niet noodzakelijk is in deze situatie.

Het tweede deel van dit proefschrift richt zich op het meten van alignement van de onderste extremiteit in 2D en 3D met behulp van een nieuw röntgensysteem, genaamd EOS. Betrouwbaarheid en validiteit van deze metingen wanneer de onderste extremiteit een knieprothese bevat zijn echter nog niet eerder onderzocht. **In Hoofdstuk 4** wordt een betrouwbaarheidsstudie beschreven waarin de intraobserver en interobserver betrouwbaarheid van EOS 2D en 3D varus / valgus (VV) metingen na rTKA worden onderzocht. De conclusie van deze studie is, dat betrouwbaarheid van zowel 2D als 3D VV metingen uitstekend is. Er bestaan echter significante verschillen tussen 2D en 3D metingen in dezelfde patiënt. Suggestie is dat deze verschillen veroorzaakt zouden kunnen worden door de invloed van de stand van het been tijdens de 2D opname. 3D metingen corrigeren wiskundig voor potentiële malpositie tijdens opname en zijn dus mogelijk meer valide. Om dit verder uit te zoeken is er in **Hoofdstuk 5** een validitiestudie uitgevoerd. Een kunstbeen met een knieprothese waarin flexie, VV en rotatie van het gehele been kon worden gevarieerd werd hiervoor gebruikt. Potentiële verschillen tussen de ware VV hoek en de hoek gemeten met EOS 2D en 3D werden onderzocht, terwijl het been in verschillende posities werd geplaatst. De resultaten van deze studie laten zien dat EOS 3D metingen meer valide zijn dan 2D metingen, hetgeen erop wijst dat 3D corrigeert voor malpositie tijdens opname en 2D niet. Dit betekent dat rekening gehouden moet worden met een verminderde validiteit van de VV hoek wanneer gemeten op een conventionele lange-been opname. Met name in het geval van een flexie contractuur, varus of valgus deformiteit of rotatie van het been tijdens opname. **Hoofdstuk 6** beschrijft een vergelijkende studie waarin peroperatieve CAS-metingen worden vergeleken met pre- en postoperatieve EOS 3D alignement metingen. Resultaten van deze studie laten zien dat EOS 3D metingen de VV hoek significant overschatten wanneer er sprake is van een uitgesproken varus of valgus deformiteit. Wanneer deze VV deformiteit niet uitgesproken is, meet CAS relatief meer valgus dan EOS. Voor de coronale meting van het tibia component is dit ook het geval. Deze bevindingen kunnen verklaard worden door het feit dat EOS 'belaste' metingen zijn en CAS 'onbelast' en mogelijke tekortkomingen in de betrouwbaarheid en / of validiteit van het CAS-systeem. Orthopeden worden geadviseerd dit in hun

achterhoofd te houden bij het uitvoeren van zowel CAS- als EOS-metingen.

Het derde deel van dit proefschrift gaat over het gebruik van CAS tijdens (r)TKA en begint met **Hoofdstuk 7**. Dit hoofdstuk beschrijft de opzet van een prospectieve klinische interventiestudie met betrekking tot CAS-rTKA in vergelijking met een conventionele techniek. Voor de conventionele techniek is gebruik gemaakt van een historische controlegroep. In primaire TKA zorgt CAS voor een verbeterde prothese alignement. Onderzoek met betrekking tot CAS-rTKA is echter schaars en het effect van CAS-rTKA op rotatie van de prothese is nog niet eerder onderzocht. Het doel van deze studie was om prothese alignement in het coronale en sagittale vlak en rotatie te vergelijken tussen CAS-rTKA en een groep waarbij rTKA is uitgevoerd volgens de conventionele techniek. De resultaten van deze studie worden beschreven in **Hoofdstuk 9**. In **Hoofdstuk 8** wordt een kwalitatieve en systematische review beschreven over de beschikbare literatuur met betrekking tot het effect van CAS-TKA op postoperatieve rotatie van de prothese. Het effect op postoperatieve rotatie van het femur en tibia component, tibiofemorale mismatch en het aantal outliers voor het femur en tibia component werden onderzocht. Zeventien studies werden geïncludeerd. Resultaten van deze review tonen geen bewijs dat CAS-TKA leidt tot een verbeterde prothese alignement als het gaat om rotatie of het verminderen van het aantal outliers. Voorzichtigheid is echter geboden bij het interpreteren van deze resultaten. Het aantal geïncludeerde studies was laag, met slechts één studie van hoge methodologische kwaliteit. Bovendien werden verschillende meetmethoden voor het meten van rotatie van het tibia component gebruikt en in slechts één van de geïncludeerde studies was de powerberekening gebaseerd op één van de uitkomstmaten van de review. In **Hoofdstuk 9** is onderzocht of CAS-rTKA een verbeterde prothese alignement geeft in het coronale en sagittale vlak en rotatie vergeleken met de conventionele techniek. In deze prospectieve studie werden 29 patiënten (31 knieën) geopereerd met behulp van CAS (CAS-rTKA). Deze groep werd vergeleken met een historische controlegroep, waarin 23 patiënten (23 knieën) geopereerd werden met behulp van de conventionele techniek (CON-rTKA). Postoperatief alignement werd gemeten door middel van EOS 3D metingen (coronale en sagittale vlak) en een CT-scan (rotatie). De resultaten tonen niet aan dat CAS-rTKA leidt tot verbeterde coronaal of sagittaal alignement of rotatie van de knieprothese of een vermindering van het aantal outliers. Het tibia component wordt echter met gebruik van CAS meer in endorotatie geplaatst, maar er is geen verschil in het aantal outliers. De bevindingen van dit onderzoek moeten met enige voorzichtigheid geïnterpreteerd worden, aangezien het aantal geïncludeerde

patiënten laag was.

De algemene discussie in **Hoofdstuk 10** geeft een overzicht en discussie van de belangrijkste resultaten van het onderzoek, zoals beschreven in de voorgaande hoofdstukken. Ondanks dat er bewijs is gevonden dat primaire knieprotheses een significant slechtere overleving hebben in vergelijking met revisie protheses, is het kiezen van de mate van constraint, het omgaan met botdefecten en het wel of niet implanteren van een steel casus-specifiek en hangt af van de ervaring en visie van de orthopedisch chirurg. Beslissingen kunnen lastig zijn, zeker wanneer er geen eenduidige richtlijnen bestaan en een groot deel van de beslissing afhangt van de peroperatieve inschatting van de orthopedisch chirurg. Dat primaire protheses een significant slechtere overleving hebben, kan te maken hebben met onderschatting van ligament- en botschade wat leidt tot het implanteren van een prothese zonder adequate constraint of stabiliteit. Ook het omgaan met botdefecten hangt af van de ervaring en opvattingen van de chirurg. Aangezien is aangetoond dat een tibia component dezelfde stabiliteit vertoont met en zonder steel wanneer een botdefect gereconstrueerd is met een TM cone, is het maar de vraag of men een steel zou moeten gebruiken.

In dit proefschrift zijn alignement metingen van de onderste extremiteit in zowel 2D als in 3D onderzocht. De validiteit van 2D metingen blijkt discutabel te zijn, maar worden toch op grote schaal gebruikt, onder andere door de uitgebreide beschikbaarheid en ervaring die er bestaat met deze techniek. Het wordt niet verwacht dat 2D metingen in de nabije toekomst vervangen zullen worden door 3D metingen, aangezien dit een financiële investering vergt. Tevens kan een 3D-systeem een 2D-systeem niet vervangen. Wanneer 2D metingen worden uitgevoerd, moet men zich bewust zijn van de validiteit ervan, zeker wanneer een patiënt een uitgesproken varus of valgus deformiteit of flexie contractuur heeft of de foto niet precies frontaal is ingeschoten.

Er is geen bewijs dat CAS-TKA rotatie van de knieprothese verbetert. Onderzoek op dit gebied is echter gelimiteerd. Ook bestaat er geen gouden standaard voor het meten van rotatie van het tibia component, wat het lastig maakt studies met elkaar te vergelijken. Behalve alignement zijn er ook weinig studies beschikbaar die de functionele resultaten na CAS-TKA beschrijven en lange termijn resultaten zijn niet bekend. Er bestaan verschillende CAS-systemen en studies over de betrouwbaarheid en validiteit ervan zijn schaars en zijn mogelijk ook systeem-specifiek. Er is geen bewijs dat CAS-rTKA leidt tot een betere prothese

alignement dan de conventionele techniek. De studie beschreven in dit proefschrift bevatte echter weinig patiënten en is daardoor potentieel underpowered. De orthopedisch chirurgen die de operaties hebben uitgevoerd vonden CAS wel een handig hulpmiddel, zeker tijdens een gecompliceerde ingreep als rTKA. Hoewel de techniek ook nadelen heeft en er nog veel onderzoek moet plaatsvinden, heeft het de aandacht gevestigd op het belang van correcte prothese positie.

De algemene discussie eindigt met de potentiële voordelen op het gebied van public health. De innovatieve technieken zoals beschreven in dit proefschrift kunnen van belang zijn voor het verbeteren van de overleving van knie protheses, het functioneren van patiënten en – uiteindelijk – participatie in de maatschappij.

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Curriculum Vitae

Marrigje Floor Meijer was born on 19 Oktober 1987 in Haarlem, the Netherlands. She grew up in Haarlem and Zandhuizen, Friesland. In 2006 she finished high school (Linde College, Wolvega) and that same year she started studying Medicine at the University of Groningen. In 2009 she received her Bachelor's degree in Medicine. After travelling through Australia and Asia, she started the Master of Medicine at the University of Groningen. From May 2010, she started her research on revision total knee arthroplasty at the Department of Orthopaedics of University Medical Center Groningen (UMCG) under supervision of drs. A.L. Boerboom. In 2011 she succesfully applied for a MD-PhD program with the research proposal 'Innovations in revision total knee arthroplasty' at the Department of Orthopaedics of the UMCG. During the course of this trajectory she combined doing clinical rotations at the UMCG and the Isala Klinieken in Zwolle with doing clinical research at the Department of Orthopaedics. From March 2011 she moved to Zwolle for a year to do clinical rotations at the Isala Klinieken. That year she finished with an internship in San Carlos, Nicaragua. In 2012, she moved back to Groningen to finish her Master of Medicine and her PhD. In July 2014, she earned her Master of Medicine. After finishing her PhD in March 2015, she started to work as a clinical resident at the Department of General Surgery at the Scheper Ziekenhuis in Emmen. It is her wish and ambition to become an orthopaedic surgeon.

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